Proceedings of
the International Symposium
on Human Genetics (1971)

Dedicated to

SRI L. BULLAYYA

Vice-Chancellor, Andhra University, Waltair (India)
who first instituted the Department of Human Genetics
and Physical Anthropology in India at Andhra University
Waltair

PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM ON HUMAN GENETICS (1971)

ANDHRA UNIVERSITY
WALTAIR (INDIA)

Edited by

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PREFACE

During the past two decades we have witnessed many impressive scientific achievements in the field of human genetics. Genetics means 'genesis' since it is the natural history of life; it means 'mechanism' of life in space and time, it means 'limit' and overcoming of limit, and it means 'synthesis' since it provides a perspective into the future. However, the last twenty-five years has encompassed the rebirth, development, and emergence of genetics as one of the most enlightening fields of biologic endeavour. Some of the oldest of man's questions have been answered and new ones posed, the vanguard of medical contributions is at hand, and the hope that some global, socio-economic problems may have a biologic solution is a possibility.

Therefore, there is some justification in publishing the proceedings of the International symposium on Human Genetics, which of necessity must be presumptuous in conception if modest in attainment.

We, as geneticists concerned with man, should see it as a part of our own responsibility not only to enlighten the public but also to promote, in the meantime, the collection, documentation, and storage of superior germinal material. If additional progress and new ideas in the field of Human Genetics are the net result, the many who have made the offering possible will consider it worthwhile.

This volume contains the scientific communications which were presented in the International Symposium on Human Genetics held at Waltair in 1971. It presents mainly a series of articles containing the current knowledge of human genetics which we believe will help the biologists, anthropologists, medical persons and human geneticists. I wish to thank my many colleagues for their kind contributions and helpful suggestions.

Department of Human Genetics
and Physical Anthropology
Andhra University
Waltair (India)
January, 1973

M. R. CHAKRAVARTTI
Secretary and Convener
International Symposium on
Human Genetics
Waltair (India)

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PROGRAMME OF THE SYMPOSIUM

Tuesday, 2nd March 71 :	Venue : Symposium Headquarters
9-00 a.m. – 1-00 p.m.	Registration of the Delegates Issuing of the Badges, Souvenirs, Programmes and the Stationery
4-00 p.m.	Inaugural Ceremony Venue : T. L. N. Sabha, Andhra University
5-30 p.m.	At Home by the Vice-Chancellor Venue : Vice-Chancellor's Lodge
8-00 p.m.	Dinner by the Reception Committee Venue : T. L. N. Sabha, Andhra University
Wednesday, 3rd March, 71 :	Venue : T. L. N. Sabha, Andhra University
9-00 a.m. - 10-00 a.m.	Lecture by Prof. Dr. P. E. Becker, Director, Institute for Human Genetics, University of Göttingen, West Germany
10-00 a.m. – 10-15 a.m.	Coffee-break
10-15 a.m. - 11-15 a.m.	Lecture by Prof. Dr. F. Vogel Director, Institute for Anthropology and Human Genetics, University of Heidelberg, West Germany
11-15 a.m. - 12-30 p.m.	Session on Human Genetics Chairman : Prof. Dr. F. Vogel Rapporteurs : Prof. O. S. Reddi (Osmania University) Dr. A. Basu (I. S. I.) Communication of papers
12-30 p.m. – 2-00 p.m.	Lunch-break
2-30 p.m. – 3-15 p.m.	Lecture by Dr. E. Schleirmacher, University of Heidelberg, West Germany
3-15 p.m. – 4-30 p.m.	Session on Clinical Genetics Chairman : Dr. E. Schleirmacher

	Rapporteurs : Prof. K. Srinivasa Rao (Andhra Medical College, Visakhapatnam)
	Dr. D. P. Mukherjee (Central Family Planning Institute, New Delhi)
5-00 p.m. – 6-00 p.m.	At Home by Faculty Club, Andhra University
	Venue : Faculty Club, Andhra University
6-00 p.m. – 7-00 p.m.	Cultural Entertainment
8-00 p.m.	Dinner by Rotary Club, Visakhapatnam
Thursday, 4th March 71 :	Venue : Assembly Hall, Andhra Medical College, Visakhapatnam
9-00 a.m. – 10-00 a.m.	Lecture by Prof. Dr. H. Walter, University of Mainz, West Germany
10-00 a.m. – 10-15 a.m.	Coffee-break
10-15 a.m. – 10-45 a.m.	Lecture by Dr. V. P. Chopra, University of Mainz, West Germany
11-00 a.m. – 12-30 p.m.	Session on Population Genetics
	Chairman : Prof. Dr. H. Walter
	Rapporteurs : Dr. A. Banerjee (Calcutta University)
	Dr. R. S. Bali (Sauger University)
	Communication of papers
12-30 p.m. – 2-00 p.m.	Lunch-break
2-30 p.m. – 4-30 p.m.	Pannel Discussion on Research Methodology on Human Genetics
	Chairman : Prof. Dr. G. G. Wendt, Director, Institute for Human Genetics, University of Marburg, West Germany
	Rapporteurs : D. C. Rao (I. S. I.)
	R. Chakraborty (I. S. I.)

Discussants :

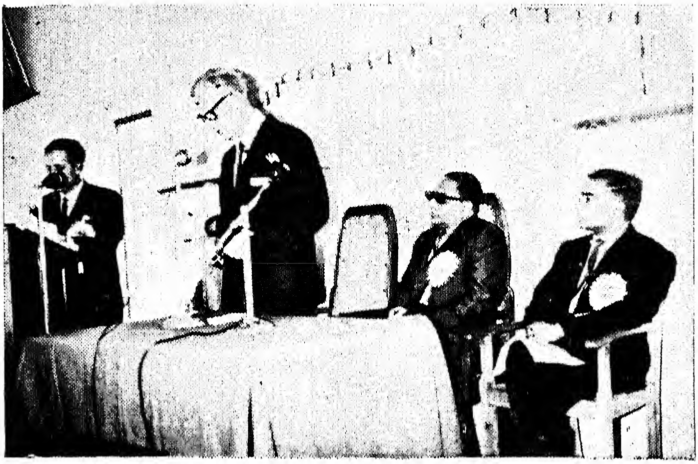
Prof. Dr. F. Vogel (Heidelberg)
Prof. Dr. W. Fuhrmann (Giesen)

	Prof. Dr. H. Walter (Mainz) Prof. T. V. Avadhani (A. U.) Prof. O. S. Reddi (Osmania) Dr. I. P. Singh (Delhi University) Prof. Indra Bhargava (Pondicherry) Dr. B. R. Murty (I.A.R.I.)
5-00 p.m.	At Home
6-00 p.m.	Cultural Entertainment
8-00 p.m.	Dinner by Anthropological Association, Andhra University Venue : Arts College, Andhra University
Friday, 5th March 71 :	Venue : Andhra Medical College, Assembly Hall
9-00 a.m. - 10-00 a.m.	Invited Lecture by Prof. Dr. W. Fuhrmann Director, Institute for Human Genetics, University of Giesen, West Germany
10-00 a.m. - 10-15 a.m.	Coffee-break
10-15 a.m. - 11-15 a.m.	Invited Lecture by Prof. Dr. H. W. Goedde Director, Institute for Human Genetics, University of Hamburg, West Germany
11-15 a.m. - 12-30 p.m.	Session on Clinical Genetics Chairman : Prof. Dr. W. Fuhrmann Rapporteurs : Dr. J. C. Sharma (Punjab) Dr. B. M. Das (Gauhati) Communication of papers
12-30 p.m. - 2-00 p.m.	Lunch-break
2-30 p.m. - 3-00 p.m.	Invited Lecture by Prof. J. Venkateswarlu, Andhra University
3-00 p.m. - 4-00 a.m.	Session on Biochemical Genetics Chairman : Prof. Dr. H. W. Goedde Rapporteurs : Dr. S. C. Tiwari (Delhi) Dr. R. P. Srivastava (Dibrugarh)

4-00 p.m. - 4-30 p.m.	Invited Lecture by Prof. K. Krishnamoorty, Andhra Medical College, Visakhapatnam
5-00 p.m.	At Home by Andhra Medical College, Visakhapatnam
8-00 p.m.	Dinner by Andhra Medical College Venue : Andhra Medical College
Saturday, 6th March 71 :	Venue : T. L. N. Sabha, Andhra University
9-00 a.m. - 10-00 a.m.	Invited Lecture by Prof. Dr. G. G. Wendt
10-00 a.m. - 10-15 a.m.	Coffee-break
10-15 a.m. - 12-30 p.m.	Session on Population Genetics Chairman : Prof. Dr. P. E. Becker, Rapporteurs : Mr. H. K. Rakshit (A. S. I.) Dr. K. C. Malhotra (Poona)
12-30 p.m.	Lunch
3-00 p.m. - 5-00 p.m.	Summary and Recommendations by the respective Chairmen and the Rapporteurs
6-00 p.m.	At Home by Lions Club, Visakhapatnam
8-00 p.m.	Dinner by Marina Club Venue : Marina Club

Welcoming the Delegates of the Symposium by Dr. D. Raghavendra Rao, Principal, Andhra Medical College, Visakhapatnam

Introducing the Symposium by Dr. M. R. Chakravartti,
Secretary & Convener



Prof. Dr. P. E. Becker (Göttingen, West Germany) speaks on behalf of the International delegates

FOREWORD

It is gratifying to know that within the past two and half decades, Human Genetics has really come into its own. The science of Genetics has come a long way since Gregor Mendel published the results of his investigations a century ago. But although the study of heredity in plants and animals advanced rapidly in the early years of our century, leading to discoveries of great value to farming and agriculture, the study of Human Genetics lagged behind. Recently, progress in Human Genetics has been rapid and extremely fruitful. Thanks to the new developments in molecular genetics, more precise ways of characterizing genetic diseases, new methods of studying human chromosomes, better family records, sophisticated statistical methods and high-speed electronic computers. Added to this is the fact that more individuals of our species are examined by competent observers than those of any other species on earth.

Human Genetics is now recognized as a highly important branch of science and medicine.

Many professional geneticists felt man such a poor animal for genetic studies – long life cycles, few children, marriages not arranged for the convenience of science – that little progress could be expected. What a change! They forgot that more individuals of our species are examined individually by competent observers than any other species on earth and selectively in that those with difficulties are preferentially examined. Here we are today, reviewing the truly remarkable progress that has been made on multiple fronts. Genetics works for the benefit of mankind, not only for today, but characteristically, for the men of tomorrow. Therefore, the First International Symposium on Human Genetics at Andhra University, Waltair, India, can express the wish and the hope that the discussions and the communications in the symposium of Human Genetics may be further steps leading toward a new, finer and happier world. I believe it is reasonable to hope that increasing knowledge of Human Genetics will benefit the human race

eventually in many ways. In recent years there have been great advances in the accuracy of genetical counselling, and the understanding of gene action has enabled previously untreatable conditions to be controlled.

The exact description of the hereditary polymorphisms in our species, which overrun the boundaries of antiquated ideas of racial groups, helps us to comprehend, rather than to deplore, each others inborn peculiarities. The social and biological values of hereditary differences are continually altering as the environment changes. We cannot be sure that any gene will be bad in all circumstances and much less sure that any gene is always good. With rapid advances of modern genetical science, new discoveries may take every one by surprise and scientists have to be continually on guard against misuse of their discoveries by those whose knowledge is incomplete. It was in the service of exchange of ideas and precise information about the nature of man that such a symposium as this was held and it was no doubt a great success. Culture and social organisation are not the ultimate forces which form us. They themselves are made possible by our genes.

This volume consists of thirty-three scientific communications which were presented in the symposium by the Indian and foreign scientists devoted to Human Genetics. They broadly fall into three categories - the clinical genetics, the red cell genetics and the population genetics. Since the contributions with regards to various categories are not well balanced, we have followed an easy method. The first six articles have been treated under the invited lecture series while the rest were considered as scientific communications presented by the Indian Scientists. We have followed the alphabetical order in arranging the articles in both groups.

Most cases which have been diagnosed as Thomsen's disease are actually those of the recessive type of generalized myotonia. Recessive generalized myotonia and dominant Thomsen's disease are two different genetic entities and the gene responsible for the defect is yet to be known. Recessive diseases are in general based on an enzyme defect while dominant Thomsen's disease is mostly due to structural abnormalities of cells or

tissues. It will be an important task to discover the basic defect for the clinical geneticists. **Becker's,** survey on non-dystrophic myotonias in the Federal Republic of Germany and Berlin presents 500 index cases of Myotonic dystrophy and 223 index cases diagnosed as "Myotonia Congenita".

His study has thrown a new light on this aspect of clinical genetics with an exhaustive critical analysis.

Chopra, studied the distribution of serum alkaline phosphatase on four endogamous groups from the Kumaon region (India). The data with regards to this field is woefully inadequate in our country and his contribution is no doubt an addition.

It should be of particular interest to evaluate the role played by the rapid disorders in atherosclerotic heart disease in India. Since the prevalence of coronary heart disease in some areas seems to be low, in general, environmental factors, here can be assumed to be rather protective against atherosclerotic disease. Serum cholesterol and triglycerides have been found to be lower in Indian population in general, but the cholesterol levels have shown an upward trend in recent years. This may be responsible in part for the noted increased frequency of coronary heart disease in the younger age groups. **Fuhrmann,** had hoped that family studies on lipoproteins with special technique would be of great general interest in our country.

While discussing some aspects of Biochemical genetics, **Goedde,** outlined two examples ; namely, the pharmacogenetic phenomenon and the inborn error of metabolism. He had raised an important question – what has to be done after detecting a new genetically determined disease? One needs a special assay for the diagnosis of atypical homozygotes and heterozygotes. Basic research, mostly with biochemical methods, has to be performed which often is the supposition for a therapy, and the different steps have to be done in team work by clinicians, biochemists and geneticists.

The importance of genetic variants for the understanding of the molecular biology of proteins has been demonstrated especially by the investigations of immunoglobulins. **Utermann,** had discussed the polymorphism of β–lipoproteins and investigated the Lp (a) – variant. Besides, the population differences

on the frequencies of Lp (a+) phenotypes, higher frequencies have been reported on the patients suffering from coronary heart disease, diabetes mellitus as well as in pregnant women, while the lower values were observed in patients, with liver diseases such as cirrhosis and hepatitis. The recent observation of Utermann, confirmed previous suggestions that Lp (a) indeed is a quantitative genetic trait. There is no isoimmunization against Lp (a) and there is no antethetical gene product known so far and the antisera has been developed against Lp (a) by immunization of rabbits with the sera Lp (a) persons.

Walter, had reviewed the distribution of genes and phenotypes of the serum protein polymorphisms like Hp, Gc, Tf, Cp and $\beta 2$ - glycoprotein I as well as Pi, the data of which are available so far from India. Though the information pertaining to the above serum polymorphisms need additional data from other populations of the world to undertake a comparison, and to establish a hypothesis, yet Walter indicated that there is a homogeneity within this country on the basis of his study of whatever could be available from India. The exact knowledge of the different serum proteins on various geographical areas would allow us to discuss a number of problems of physical anthropological origin as well as of the biology of human population.

The growing development and utility of palmar flexion creases and palmar dermatoglyphics in Anthropology, Human Biology, Medical Genetics has fully been recognised. **Bali**, had raised a problem - whether persons affected with certain diseases are distinguished from the non-diseased by characteristics of palmar flexion creases. Association of Simian crease with Schizophrenia has already been on record while an attempt has been made to establish the probable relationship between the schizophrenic patients and the controls on the basis of all palmar creases. The association suggests a parallel development of genetical factors between creases and schizophrenia.

Banerjee and Das Chowdhury, had discussed on the genetics of quantitative characters of human head hair. Morphological characteristics of human head hair as one of the criteria for racial study has long been recognised. How far the different histological characters of hair shaft are controlled by the gene-

tic component of variability and how far by the non-genetic ones has yet to be thoroughly investigated. A strong hereditary component of variability has been found to be responsible for the incidence of all the quantitative characters of human head hair.

Marriage distance is an important variable in human genetics, for, it determines the extent to which a given gene is expected to move per given unit of time. **Basu**, raised a vital question in exploratory study of marriage distance among the Santhals of Bihar, India. In case of humans, physical movements are not necessarily followed by mating, so that a comparable study should refer to physical movement consequent upon marriage rather than physical movement as such. The probability of marriage seems to be determined by many factors as mentioned by Basu. He had proposed some possible explanations for the distribution he obtained and had compared the same with those obtained elsewhere. A sophisticated explanation for the difference had been attempted.

Ethnically the Tibetans constitute a heterogeneous stock of people. It is, therefore, not unlikely, if a defferential fixation of allele frequencies is revealed within the Tibetan racial complex. **Bhalla**'s blood group data on the three groups of Tibetans were processed with a view to ascertain variations in allele frequencies with regards to the above. The results reveal some interesting trends of gene frequency variation in Tibet.

Although random references to genetic drawbacks of consanguineous marriages have been made, yet their relationship with chromosomal aberrations had not been confirmed. The high incidence of consanguineous marriages in Pondicherry (Tamil Nadu, India), provided **Bhargava et al**, an unique opportunity of testing Penrose's (1961) hypothesis of recessive genes causing non-dysjunction in ova of homozygous females. The high frequency of trisomic syndromes in children born of young mothers, married to their maternal uncles, apparently lends support to Penrose's hypothesis and disagrees with other reports from Sweden, Japan and U.K.

Andhra Pradesh especially the coastal part of the state provides a fertile and rich field for populational genetical studies because of the presence of innumerable tribes and castes.

The tribal concentration of the state is about 4.5% of the total population of the state. **Busi**, presented a study of some genetical markers among the two predominant tribal groups of Coastal Andhra Pradesh. There appears to be very insignificant biological diversity between these two groups. Studies specifically directed to test the assumption of homogeneity of populations are few but do exist in the published literature which throw significant light on the problem by showing demographically the occurrence of sub-populations within a population.

In population genetic studies, the estimation of gene frequencies largely depend upon the assumption of random mating. But this assumption is quite serious since any deviation from it will attach no physical meaning to the estimates. **Chakraborty**, in his paper proved a theorem showing that such a declaration (that whenever in a population ABO blood group phenotypes are seen as $p+q+r=1$, one should not think that the population is under panmixia) will often be erroneous. The same can be extended to any phenogram analysis where the genotypes are indistinguishable from one another.

In view of the current interest in the problem of detecting inbreeding magnitudes in natural populations, **Chakraborty and Rao**, considered the problem with reference to ABO blood groups data dealing with characters that involve dominance relationships. The basic line of approach was through a consideration of the power of non-central χ^2 test to detect deviations of phenotypic proportions from Hardy - Weinberg proportions.

Das, studies the taste sensitivity to phenylthiourea among the four divisions of the Khasi of North-East India. The data were analysed to find out the inter-division relationships which were not significant.

Studies on palmar ridge counts were neglected for a long time until Fang (1950) studied the inheritance of a–b ridge count. As Pons (1964) concluded that a–b ridge count is due to polygenes with additive effect. A review of a-b, b-c, c-d and a-d ridge count in different populations could be attempted by **Chattopadhyay**, as a marker for studying population variation.

It is now well-established that the biological variation among the groups are caused by processes such as mutation,

selection, migration, genetic drift and hybridization. **Malhotra's** extensive study gave further empirical support to Karve's hypothesis of Caste origin. The genetic heterogeneity observed in various endogamous groups need not be due to genetic drift.

The simple dichotomy of the Rh blood group phenotypes into Rh-positives and Rh-negatives has still its importance in clinical obstetrics and blood transfusion. Keeping this importance in view, **Mukherjee**, had attempted to estimate an overall Rh-negative incidence rate for the Bengali Hindus (2.910 ± 0.192 per cent), based on the data available from literature. Possible incidence rates of haemolytic disease in the new born of the same group had also been estimated and found to be 12 to 25 per 10,000 pregnancies.

A new method using 3 mm. filter paper strips has been devised for collecting blood samples for red cell LDH isozyme variants by starch gel electrophoresis by **Mukherjee and Das.** The method was found to be of significant advantage in mass screening of LDH variants present in erythrocytes.

Murty and Rajya Lakshmi, had discussed the results of a sample survey undertaken in the newly developing areas of the twin cities of Hyderabad and Secunderabad wherein most of the immigrants from Coastal Andhra and Tamilnadu had settled. In the average each family had a sex ratio of ♂ 1 : 1.08 ♀. The average family size was higher in Brahmins (4.23) than in Non-Brahmins (3.32). There was no positive indication of the presence of incompatibility in the population.

The concept of genetic load was first developed by Haldane (1937) who considered it as the cost to a population's total reproductive potential for having genetic variation in fitness. The incompatibility load due to Rh factor in small population is due to the interaction of selection against heterozygotes born to recessive mothers, mutation to the Rh factor and random drift. **Prem Narain** had developed this theory in a finite population.

Sickle cell trait provides a valuable marker in determining the genetic relationship between the major tribal population of India. **Negi,** reviewed the distribution of this trait in respect of the non-mongoloid tribal populations of India. Among

the 'Gond' groups it varies between 13.46% and 19.38% while the 'Bhil' group presents this trait as high as 26.60%. The striking absence of sickling in Austric speaking population is interesting.

Sen and Singhrol, had presented a report on the ABO blood groups and ABH secretion of Bade Bhinjhwars of Chhattisgarh (M.P.). A planned and well designed study may throw further light on the genetic relationship of the major tribes of 'Gond' group.

Sharma, presented a large pedigree to throw additional light on the wide range of variability that exists in the pleiotropic character associated with the inheritance of mental defects and neuromuscular-disorders and tried to explain the mode of heredity and possible role of environment in the manifestation of these disorders. The pedigree offered some evidences that the genetic factors for the diseases are carried on the autosomes and behave as recessive and dominant recurrently. This dual behaviour may be due to psychological or socio-economic factors which may have triggered the onset of the disease.

While studying the dermatoglyphic patterns in Mongols, **Satpathy,** was of opinion that the palmar and hallucal patterns, as suggested to be typical of Mongols, were more frequent in those born to elderly mothers. As translocation Mongols were commonly born to younger mothers, the study, suggested that the dermatoglyphic patterns were also less pronounced in translocation Mongols than the trisomy ones who were usually born to mothers at an advanced age. It is, however, necessary to confirm this by chromosome studies.

Andhra Pradesh with its high rate of inbreeding forms a rich and fertile field for studying the inbreeding rate and the biological effects of inbreeding in population; especially for genetical counselling. **Veerraju,** presented a survey of inbreeding in rural areas of Coastal Andhra Pradesh. He recorded an incidence of about 39.1% of consanguinity out of all marriages. The frequencies of the various consanguinity classes also show strong social and geographic stratification. An important problem in studies of consanguinity is therefore the proper

choice of non-inbred controls. As such, a prospective study with regards to consanguinity would be a suitable selection of the problem. In this prospective study, matings will be chosen for study because of their consanguinity. The best way to choose controls for such study is probably to take married sibs of the consanguineous mates, provided these are not themselves consanguineous with their mate and provided they have not moved to other areas. This choice greatly reduces the probability of bias, but also decreases the sensitivity of the test, because there is a higher probability that the progeny of the sibs of the consanguineous mates are affected by the same diseases as the progeny of the consanguineous mates than that the progeny of the population at large are. It is expected that, a collaborative research, on this line, between Andhra University and German Universities will mature soon.

Venkateswara Rao investigated the influence of smoking on arterial pressure and observed that smoking increases both systolic and diastolic pressures, usually between 6–10 mm/Hg. The pulse rate also behaves in the similar direction.

The recognition of the increased incidence of Down's Syndrome with maternal age was an important step in the direction of the cause of spontaneous mutation. Because Down's Syndrome is due to a chromosomal aberration rather than a specific gene mutation. It is an example of an effectively dominant defect. A few instances of reproduction by individuals with Down's Syndrome are known, and among their offspring the expected 1 : 1 proportion of affected is found.

Their fitness is so low, however, that practically all cases, at least for the 47-chromosome type, are the result of fresh mutation, more exactly, of non-disjunction in one of the parents, almost always the mother (Penrose and Smith, 1966). **Satyanarayana**, presented a very interesting account on Down's Syndrome in Coastal Andhra Pradesh. In contrast to Penrose's study (1939) he stated that a Mongol need not be the last child of a large family as he found half the cases were first born. His study revealed that the trisomy of 'G' group was the commonest aberration while translocation and other atypical cell lines could not be observed. Although the material presented by him were very scanty but at the same time some signi-

ficant and pertinent observations would inspire us to follow up the study with a large series from this part.

A series of five very interesting communications were received from **Srinivasa Rao** of Andhra Medical College, Visakhapatnam, which assures us of a very promising field of clinical genetics in our country. A typical case of Klinefelter's Syndrome characterised by small testes with Azoospermia, Gynaecomastia and chromatin positive male who showed a 47/XXY chromosome complement. This could not be detected until they reach puberty or later in the clinics.

Alkaptanuria is a simple autosomal recessive trait, although pedigrees showing dominant inheritance are also on record. A case of Alkaptanuria with autosomal dominant gene without any history of consanguinity was presented by the same author. The case manifested ochronosis, arthritis and Spondylosis, besides Alkaptanuria. A clinical history was also attempted.

A case of Gaucher's disease confirmed by bone marrow study, splenic smear, liver biopsy and histopathological studies was reported by **Srinivasa Rao.** The genetic and familial predisposition of the disease was discussed with the pedigree showing the recessive heterozygous parents and the homozygous affected siblings who manifested the disease process. He remarked that the Gluco-cerebrosidase enzyme deficiency is the ultimate enzyme factor which is the 'inborn error'.

In the two subsequent papers, **Srinivasa Rao** presented a rare tumor of Gonadoblastoma in a dysgenetic gonad with inter sex and chromosomal pattern of XO/XX/XY and a case of familial XY female with Testicular feminisation Syndrome were presented.

The sexual dimorphism is undoubtedly the most important of all human polymorphisms and provides the most direct example of a simple Mendelian segregation. The existence of sex is one of the most significant factors influencing our biological and social organization. Testicular feminization provides an interesting paradox for sex-linked inheritance. Sex-chromosome abnormalities constitute about one-fifth of all chromosomal anomalies observed at birth (Court-Brown, 1967). The majority are either XXY; XO or XYY, though it is not easy to get reliable unbiased estimates of their frequency at birth.

Research in Human Genetics is alive with excitement and revolutionary advances. Important to the development of science and to the evolution of social structure, genetic thought is widening its impact on many areas: immunology, protein chemistry, cellular physiology, developmental biology, medicine, agriculture and industry. So many partnerships and such rapidly expanding methodology demand a fresh approach to genetic training especially in our country. The World Health Organisation during the last two decades, through its expert committees, have emphasized the need for inclusion of the study of Human Genetics in the curriculum of medical students and in the Universities. The study of Human Genetics has been gaining momentum in many parts of the world. Physical Anthropologists of our country are deeply interested in the study of Human Genetics.

It is with this impetus, the Andhra University has started for the first time in the country a Department of Human Genetics and Physical Anthropology from this year (1972).

Writing a foreword for the book Containing thirty-three articles presented in the symposium requires genes. The editor's genetic endowment in writing is modest but luckily he enjoys generous and able guidance and cooperation from Sri L. Bullayya, Vice-Chancellor, who created this Department of Human Genetics and Physical Anthropology and encouraged him to re-investigate the meaning of human heredity in this country. His encouragement emboldened the editor to undertake this task.

Inaugural Address

by

Sri L. BULLAYYA

Vice-Chancellor, Andhra University

Waltair

INAUGURAL ADDRESS

SRI L. BULLAYYA
(Vice-Chancellor)

Ladies and Gentlemen,

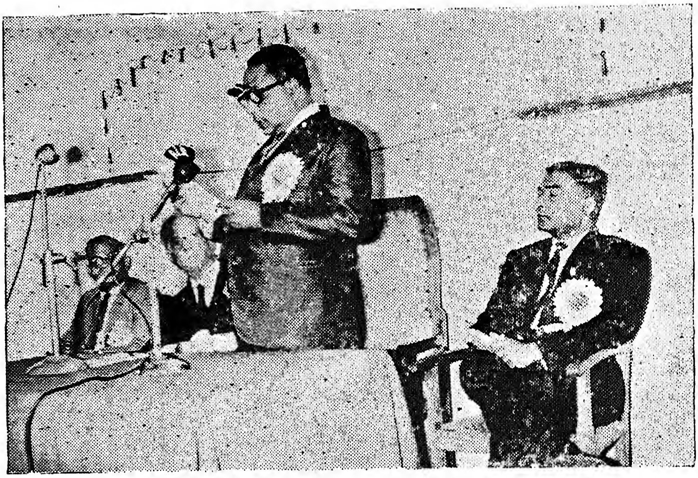
It is with great pleasure that I welcome you, the delegates and visitors attending this International Symposium on Human Genetics, to this campus. Some of you must have gone round the University and perhaps you have already formed ideas about the general organization of our various Faculties. With the limited resources at our disposal, we are trying to work up a scheme of priorities and development which would yield the maximum results at the postgraduate level of studies. During the last two years, we have been attempting to build up a School of Life Sciences with the nucleus of Botany and Zoology, which are two of our major Faculties. Next year, the Department of Bio-Chemistry will start functioning and soon we expect to add Bio-Physics, Microbiology and Radiation Biology; and in this setting and programme, you will see how great is the significance of your Symposium, for its discussions may shape the constitution of yet another unit in the Life Sciences, and a most vital unit, which will attempt to throw light on the extraordinary miracle of life, which is studied under heredity or genetics. The marvel of the creative process in nature has been so baffling and overwhelming that it could be explained only in terms of a divine function. For ages together religion and church had a monopoly of this miracle; and only during the last hundred years has any attempt been made to view it as a scientific process capable of a functional explanation. The middle of the 19th century was a water-shed, which started the era of modernity; and the first of its great impulses was that of the Darwinian theory of Evolution.

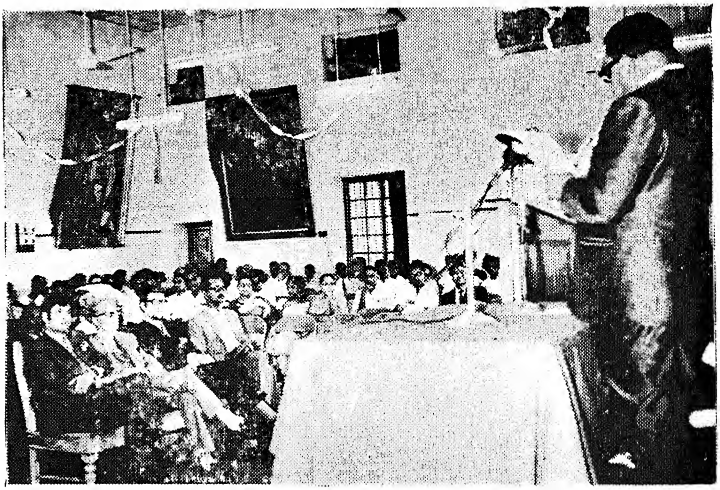
Early thought on the subject of study of Genetics was mainly speculative and it was even believed that there was a continuity of certain hereditary characteristics as developed in animal breeding; but it was presumed that acquired characteristics

also could be inherited. Mendel perhaps is the high-priest who postulated the theory of immortality of the germ plasm and so developed a Theory of Heredity by the chromosomes. His central idea of inheritance through certain determinants seems to have held the ground all through ; and yet another name is that of Galton, who inunciated the Law of 'FILIAL REGRESSION' by statistical methods and proved certain external characteristics applicable to large groups of populations. Bateson and his colleagues coined the term 'genetics' to designate that portion of Biology dealing with heredity, variation and evolution, and to throw light on the resemblances and differences shown in plant or animal related by descent, and how the characteristics of parents and offspring are related, and how these of the adult lie latent in the egg and how they become patent as development proceeds. The chromosomes within the cell of the organism carry the most important factors which control the life of the cell, and these factors are passed on from one cell to its daughters as hereditary factors.

All living things eat, and mate, to perpetuate their species. The animal processes are varied and perplexing, and the mutations that arise in their growth are so numerous that it could all be explained only as an act of God. And this is subject to yet another influence, that of time; which has little or no effect on non-living creatures. The measurement of time applicable to life is slower and indicates the change from parent to offspring and it extends from one generation to another; and the study of this is 'genetics'—one of the most central aspects of Biology. There is, however, a wider time-scale applicable to living things—from generation to generation and from one age to another slow changes come about through various influences and this is the process known as evolution; and the study of the evolution of man in his whole history and civilization constitutes the scope of Anthropology.

I am only trying to sort out how in Life Sciences or Biology, Anthropolgy has a place and how genetics is the most valuable field of investigation to throw light on man and his growth from generation to generation. This is the field with possibilities of inexhaustible study, which is opening before you when you apply yourself to the science of Genetics, here applied to human





Inaugural Address by Sri L. Bullayya, Vice-Chancellor, Andhra University

Participants and Guests attending the Inaugural Ceremony at T. L. N. Sabha, Andhra University

species. It is altogether a new field and we are making only a small and tentative probe into this mystery. It therefore angurs well that and the Andhra Medical College, has joined hands with the Department of Physical Anthropology and Human Genetics to pool their scientific resources to this subject.

Our Department of Anthropology is comparatively young, just ten years old. It has at present a staff of six teachers and four research fellows and several research scholars who are working on different problems of Human Genetics and Physical Anthropology. Last year, with the help of some eminent scientists from abroad, the Department organized six Seminars on various aspects of population and Clinical Genetics. They have currently rasearch collaboration with the Universities of Bonn, Heidelberg and Mainz in West Germany on some aspects of Human Genetics for which rich and abundant material is available in the different population groups in this part of the country. The co-operation of the Medical Faculty will enhance the value of such research and enable some advances into the modern Genetical science and exchange of ideas on many of these vital problems. Last year, there was a National Congress on Human Genetics at Poona, which aroused the interest in the subject in our country : and the late J. B. S. Haldane, R. R. Gates and Curt Stern carried out pioneering research in this field in this region of India and all this will assist us to formulate a programme for such an intensive study of Human Genetics as a Faculty in our University. A Symposium like this, in which eminent men in this speciality of Human Genetics are participating, will serve as a stimulating background for our own scholars and scientists to move in the matter. This will fit in well with our general plan of developing the School of life Sciences; and the University is therefore most grateful to the distinguished scientists who have assembled here to give thought to this new subject of Human Genetics.

It is with pleasure that I welcome you to this Campus and inaugurate your deliberations. I hope they will be fruitful and far-reaching and pave the way for constituting a new Faculty in our University. Thank you.

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Visiting Professors

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International Symposium on Human Genetics,
Andhra University, Waltair, March 2 - 7, 1971, pp. 1 to 24

NON-DYSTROPHIC MYOTONIAS
(A PREVIOUS SURVEY)

P. E. BECKER
(Director, Institute of Humangenetics, University of Göttingen,
West Germany)

Myotonias are an under developed territory in which the seperation of genetic entities is disputed. Even today the opinion is stressed occasionally that the three well-known myotonic diseases "Myotonia congenita"(Thomsen), "Paramyotonia congenita" (Eulenburg) and Myotonic dystrophy (Curschmann Steinert-Batten) are only clinical variants of one and the same myotonic disease. A clear distinction is rendered even more difficult by the fact, that these three genetic types all show dominant inheritance and that the basic gene-depending defect of all three diseases is still unknown. Nevertheless there is no doubt, that the three myotonic diseases mentioned are not only different genetic types, independent one from another, but that there are even more genetic types of myotonia. Myotonia is a symptom and not a disease.

By an inquiry of neurologists and internists and of neurological and internal departments of hospitals and university clinics in the German Federal Republic and in Berlin I collected about 500 index cases of Myotonic dystrophy and 223 index cases diagnosed as "Myotonia congenita".

I did not examine the cases of Myotonic dystrophy, if the diagnosis seemed to be certain, because, as you know, there a re several fundamental genetic investigations of this dystrophic type (Thomsen 1948, Lynas 1957, Klein 1958). Therefore I concentrated my interest on the rarer non-dystrophic types of myotonia.

A survey of the index cases is presented in Table 1. Among those diagnosed as "Myotonia congenita", in 20 cases the

revised diagnosis after examination was Myotonic dystrophy. I never saw a relative with Thomsen's disease or any other type of myotonia apart from Myotonic dystrophy in the families of propositi with Myotonic dystrophy. On the other hand, in the families of index cases with the confirmed diagnosis of non-dystrophic myotonia I never found a patient with myotonic cataract or dystrophic alterations typical for myotonic dystrophy. Both diseases, Myotonic dystrophy and Myotonia congenita could not be observed in one and the same family.

TABLE 1

Results of the inquiry of neurologists and internists in the German Federal Republic

		Index cases
I "Myotonic dystrophy"	about	500
II "Myotonia congenita" (non-dystrophic myotonias)		223
Revised diagnosis :		
Myotonic dystrophy		20
Myotonia congenita (Thomsen)		28
Recessive generalized myotonia		97
Sporadic and sibling-cases with generalized myotonia classification doubtful		16
Paramyotonia congenita		6
Periodic paralysis with paramyotonic signs and myotonic symptoms		5
Myotonic symptoms in combination		
with strumectomia		1
with Adie-Syndrome		1
Myotonia paradoxa		2
Doubtful myotonic syndrome		1
Neuromyotonia (Mertens) or "Myokymia, myotonia and increased perspiration" (Gamstorp and Wohlfart)		3
Non-myotonic diseases		15
Examination refused; residence in foreign countries; not detectable; died		28
		223

In a special single case, however, the real diagnosis can be difficult at first sight. For example: the patient in figure 1 consulted me because of infertility. At first sight one could have taken him as a Thomsen case – his muscles are well developed and myotonia is generalized. Testicular atrophy with oligospermia, however, and a beginning myotonic cataract corrected this false diagnosis.

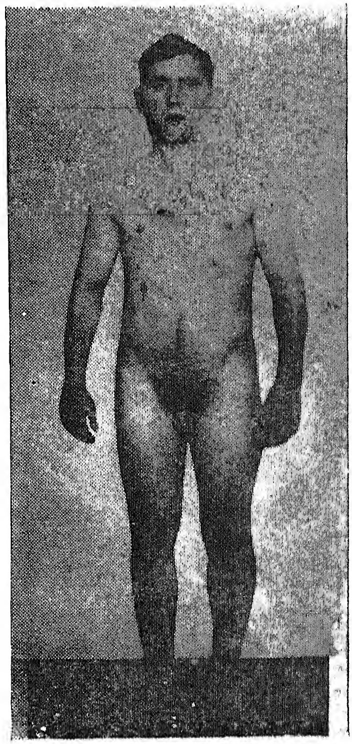


Figure 1

In myotonic dystrophy myotonia and muscular atrophy are symptoms like cataract, testicular atrophy, frontal baldness and many others, while Myotonia congenita or Thomsen's disease is a real myopathy, as far as I see, without any affection of other organs and tissues.

In the original family of Dr. Asmus Julius Thomsen who gave his name to this disease 69 myotonic persons are known (fig. 2) Dominant inheritance is clearly to be seen. I had the opportunity to examine seven affected relatives of Dr. Thomsen. Myotonia has been transmitted in this family through eight and nine generations.

Including Dr. Thomsen's family I could investigate 28 families with regular dominant transmission in the Federal Republic. I counted 151 patients and 192 unaffected among the children of affected persons (with omission of the sibship of propositi). This number of 44 ± 2,7 to 56 ± 2,7 % coincides with the expected ratio of 50 % : 50 % in regularly dominant Transmission. In the 28 pedigrees no generation has been skipped.

Both sexes are almost equally often affected. The ratio between male and female patients is $54 \pm 4{,}1\ \% : 46 \pm 4{,}1\ \%$. Myotonia usually appears in females in a milder form than in males.

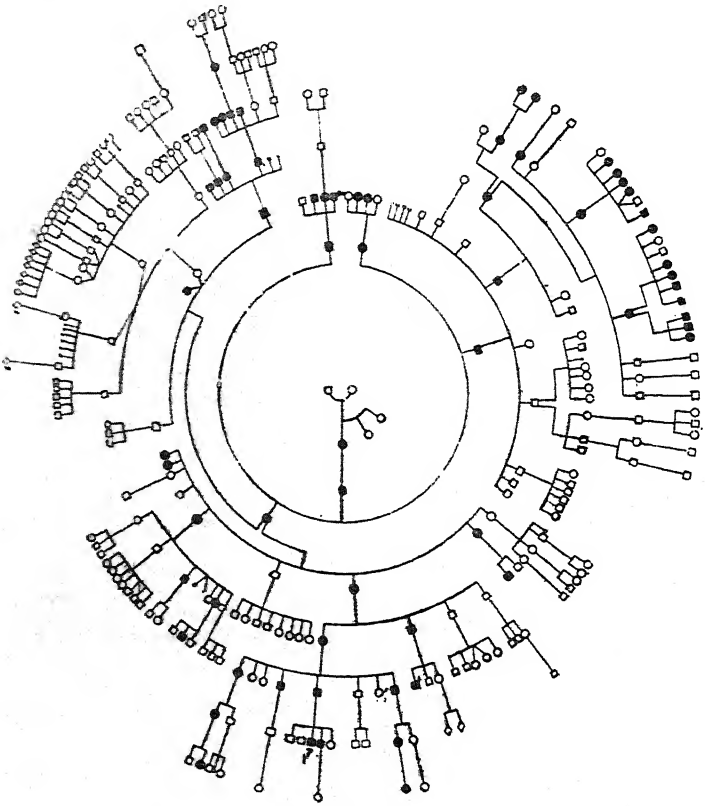


Figure 2

The disease, as the epithet "congenita" says, can be noticeable soon after birth.

I could examine 114 persons of dominant Thomsen's disease. Percussion-myotonia of the tongue figure 3 is a regular finding; only in 8 of 114 cases it was lacking. Myotonia is often generalized. Sometimes, however, it is manifested only slightly.

Dr. de Jong in Heerlem has examined a family with dominant myotonia in the Netherlands. In this family all affected persons had a weak manifestation. In some cases only a mechanical myotonic reaction of the tongue and a slight stiffness of the fingers after making a fist were stated. Dr. de Jong speaks of "Myotonia levior" and has stressed that this is an independent genetic type, different from Thomsen's disease. In the original family of Dr. Thomsen I have seen two patients with the same slight myotonic symptoms like those in the family of Dr. de Jong. These two affected persons did not know that they had Thomsen's disease. Such a slight maifestation can often be found in families with Thomsen's disease in which other relatives are more severely affected. So I have some doubt, whether there exists a special type of "Myotonia levior" different from Thomsen's disease. As a rule the examinations in families with Thomsen's disease shows that the manifestation is generally more slight than one would expect from the literature, which offers a selection of severe cases. Let me say here, that most cases reported in the literature are not those of the real Thomsen's disease but of Recessive generalized myotonia about which I shall speak later.

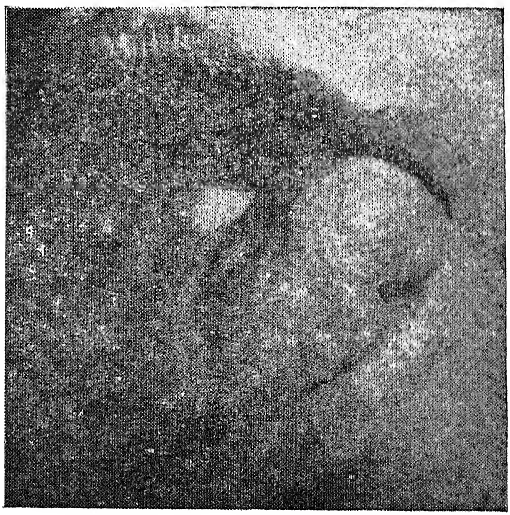


Figure 3

Cold aggravates myotonic symptoms, but not in all patients with Thomsen's disease. In some families cooling is a very important aggravating factor at least in most cases, but there

are patients in the same families without any influence of coldness, specially those who are only slightly affected.

In Thomsen's disease a distinct muscular hypertrophy is rarer than it is to be expected according to the pictures in text- and hand-books. Only a small proportion of all cases show a real muscular hypertrophy. The great majority exhibits only well developed muscles, as figure 4 demonstrates, which shows 10 unselected propositi with Thomsen's disease. Those patients with muscular hypertrophy are in general most severely myotonic.

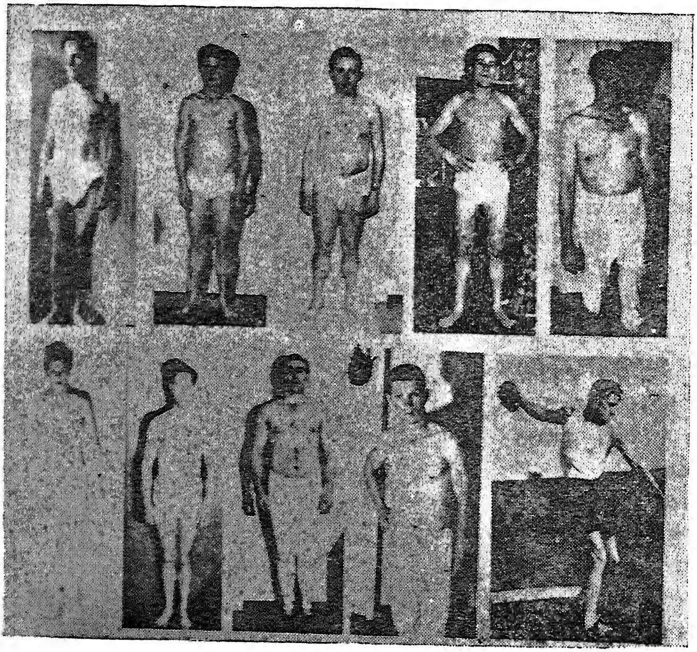


Figure 4

Thomsen's disease usually remains unchanged from birth on through life. However, several older persons have the impression that myotonia has improved with progressing age. In many cases, however, it was not clear whether myotonia has really improved or whether the patients had learned to adapt

better and to avoid strong muscle efforts – But myotonia can undulate in the course of life. Some patients are temporarily more hampered, at other times they are nearly free or only slightly myotonic. Some female patients have experienced that myotonia may become more severe during pregnancy.

The residences of the eldest known patient of each family with Thomsen's disease are pointed out on the map figure 5. As you can see, there is no accumulation in a geographical district. I am sure that I did not find out all cases of Thomsen's disease by the inquiry, because most affected persons never

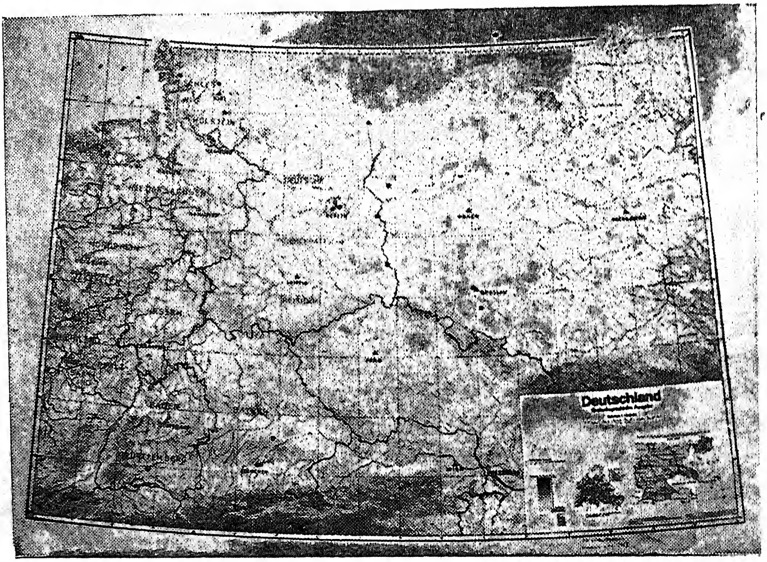


Figure 5

consult a doctor on account of their muscular abnormality and even when they need medical aid in other respects, they rarely mention their myotonic symptoms. Myotonia in Thomsen's disease is considered to be a troublesome but harmless anomaly or family peculiarity, the sufferer has to tolerate it or has to make best of it as did his ancestors. Occasional experience of medical ignorance and therapeutic helplessness concerning myotonia confirmed this opinion. In the whole there is a

strong tendency among myotonic persons to hide their family anomaly as well as possible, because occasionally it has exposed them to ridicule or has led them to shameful situations. In many other cases myotonia is so slightly manifested, that the affected person does not give regard to it. Under these circumstances it is impossible to ascertain the frequency. It is my opinion that the families which came to my knowledge make up only a small proportion of all persons with Thomsen's disease living in the Federal Republic.

In slightly affected persons the initial myotonic inhibition is so trifling that they are not really hampered and on the other hand the strongly developed muscles enable them to peculiar efforts. In any case it is remarkable that many slightly affected persons go in for sports, have taken part in sporting contests and achieved results above the average in gymnastics. One could imagine that slight myotonia had a selective advantage in earlier times, when muscular strength was of importance for fitness. The 28 propositi and their families with Thomsen's disease in two or more successive generations make up only a small proportion of all cases with generalised non-dystrophic myotonia, diagnosed by colleagues as "Thomsen's disease". The next slide shows that 69 propositi are sporadic and that in 44 cases only siblings are affected, whereas parents and children are healthy. The parents of the propositi, however, could not be examined in all cases, because they were not more alive. Therefore dominant transmission could not be excluded in each case. In about 16 families of sporadic and sibling cases Thomsen's disease can not be fully excluded. But apart from these 16 families the resting 59 sporadic and 38 sibling cases need an explanation. One could suppose that the sporadic cases are new mutants of Thomsen's disease. This hypothesis, however, must be dropped, if one considers that the mutation rate would be improbably and inexplicably high, if all sporadic cases or only the majority of them were new mutants. In addition the numerous sibling cases would need an explanation. Therefore the only plausible explanation is that the diagnosis "Thomsen's disease" is applied to heterogeneous cases, and that a recessive type of generalized myotonia exists besides the dominant Thomsen's disease.

The existence of a recessive type of myotonia is confirmed by the proportion of affected to non-affected among the siblings of the 97 propositi with healthy parents and children. The value is between 18% and 28% (according to the supposition of single case selection and of family selection), being in agreement with the expected 25% in recessive inheritance.

A further proof of the recessive type is the increased number of blood related marriages among the parents of patients which amounts to 12%, 5% of these being first cousin marriages. This is about 10 times the frequency of first cousin marriages in the random population. In one case a myotonic patient is the product of an incestuous relation between father and daughter. In four other cases distant blood relationship is suspected.

The ratio of sporadic to sibling cases is in agreement with recessive heredity too. After having proved the existence of a recessive type of myotonia, one could expect that there may also be clinical differences between the recessive type and the dominant Thomsen's disease.

Concerning the onset of myotonic symptoms the real Thomsen's disease seems to bear the epithet "congenita" for good reason. Figure 6 demonstrates that myotonic signs were noticeable within the first three years of life in about 1/3 of the cases of dominant Thomsen's disease which I examined. One can suppose that in the rest of cases the myotonic susceptibility was also present from birth on, but that myotonic troubles were remarked and noticed in school time, for instance in gymnastics for the first time. In some cases the earliest myotonic signs were clearly recognizable in adult age, for instance by a strong effort. This is plausible, if one has in mind that in 15 persons myotonic symptoms could be established by my examination for the first time and that myotonic susceptibility is variable, so it can be un-remarkable at times at least in some cases.

On the other hand in recessive myotonia (fig. II7) the onset seems in general to be somewhat later, in the majority at an age of 5 to 10 years. In contrast to Thomsen's disease the onset seems to be gradual. In about half of the cases the legs are the

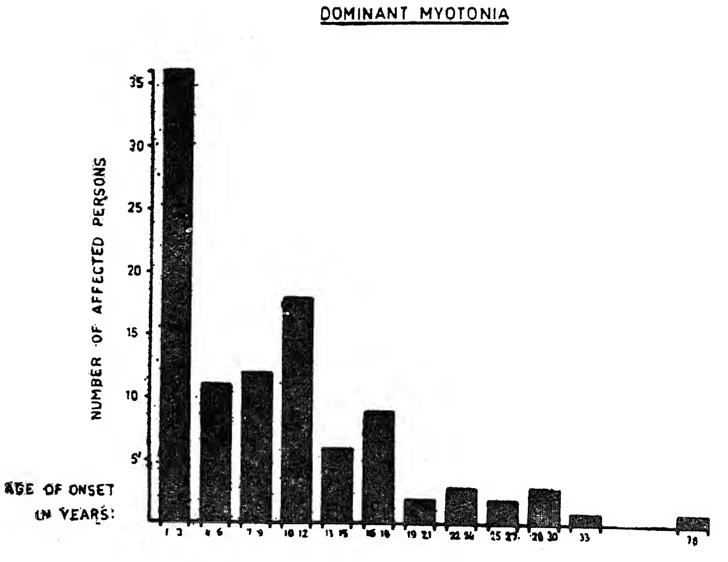


Figure 6

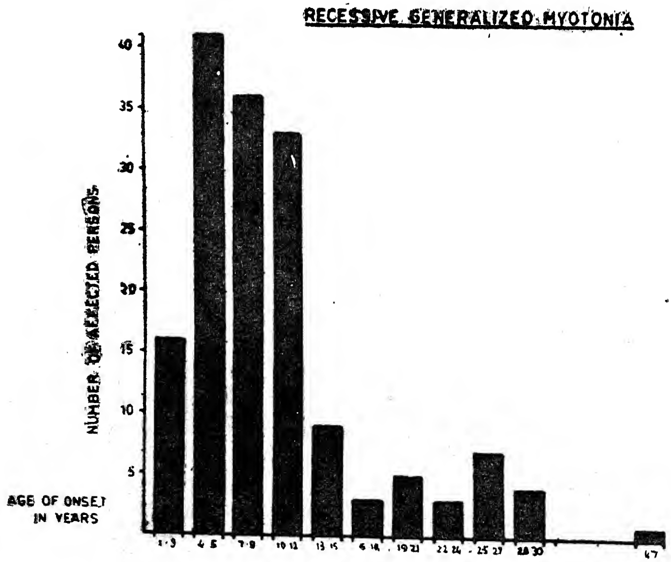


Figure 7

first to be affected and only after some years myotonic troubles of the hands and arms occur. At last the chewing muscles, the lavator palpebrae and the orbicularis oculi are affected. But in other cases myotonic signs were recorded to be present in the whole musculature as long as the patient could remind.

The most important clinical difference between Thomsen's disease and Recessive generalized myotonia is, that patients of the latter are on the average more severely effected than those of the former type.

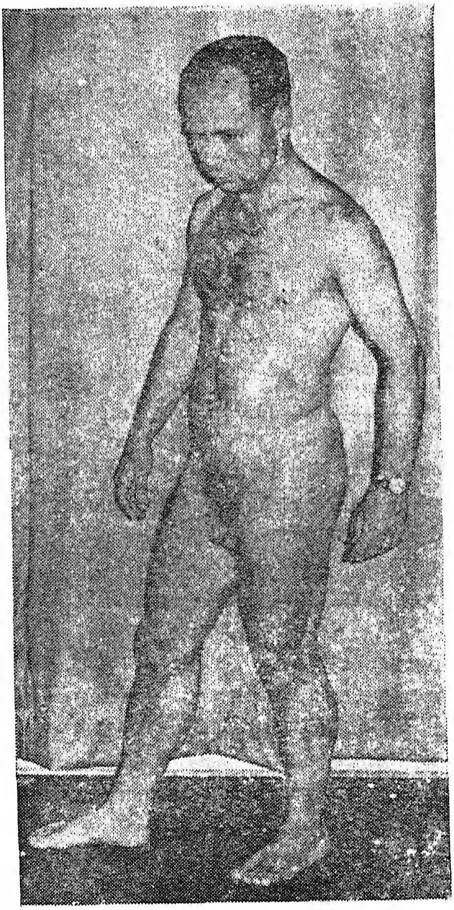


Figure 8

Muscular hypertrophy is more accentuated in the recessive type. In Thomsen's disease most patients have, as I said, well developed muscles but not real muscular hypertrophy. I suspect that the pictures of patients with enormous hypertrophy belong to the Recessive generalized myotonia and not to Thomsen's disease. The figure 8 presents a typical case of Recessive generalized myotonia. The gait is initially hampered but also by walking it gets not always completely loose. The following figure 9 demonstrates that muscular hypertrophy can be present already in childhood.

The hypertrophic muscles are unusually firm, even in relaxed condition. The dorsal flection of hands and feet is almost limited. Hollow feet often occur.

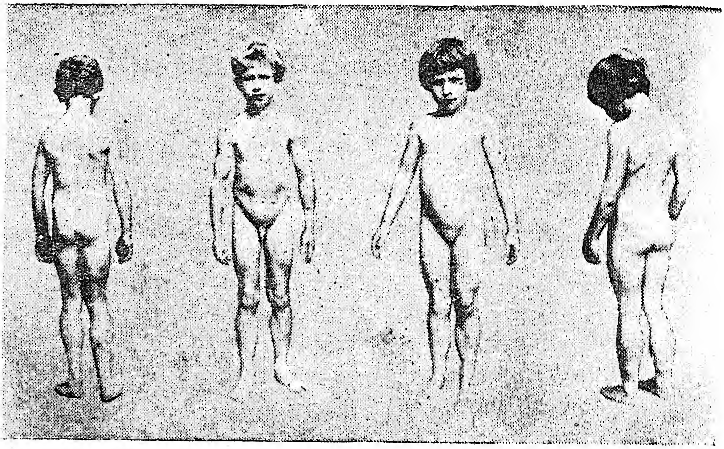


Figure 9

A further important difference compared to Thomsen's disease is to be seen in the muscle strength; in recessive myotonia muscular weakness is often striking in spite of hypertrophy. It diminishes the working ability often more than myotonia itself. In several cases I observed a remarkable diminution of muscle volume in the lower third of the forearms (fig. 10). Only in rare cases, however, there is a distinct atrophy of the forearms and of the sternocleidomastoid muscles and most exceptionally of the small hand muscles too. On the other side, the leg muscles and the shoulder girdle muscles are generally hypertrophic. It seems to me, that such cases have been regarded for transitional cases to myotonic dystrophy occasionally. But they neither have myotonic cataract nor other dystrophic signs which characterize myotonic dystrophy. Recessive generalized myotonia and Myotonic dystrophy are different genetic types with different mode of transmission without any interrelation.

In the biopsy (fig. 11) of the forearm muscles of some patients with Recessive generalized myotonia Dr. Kuhn and

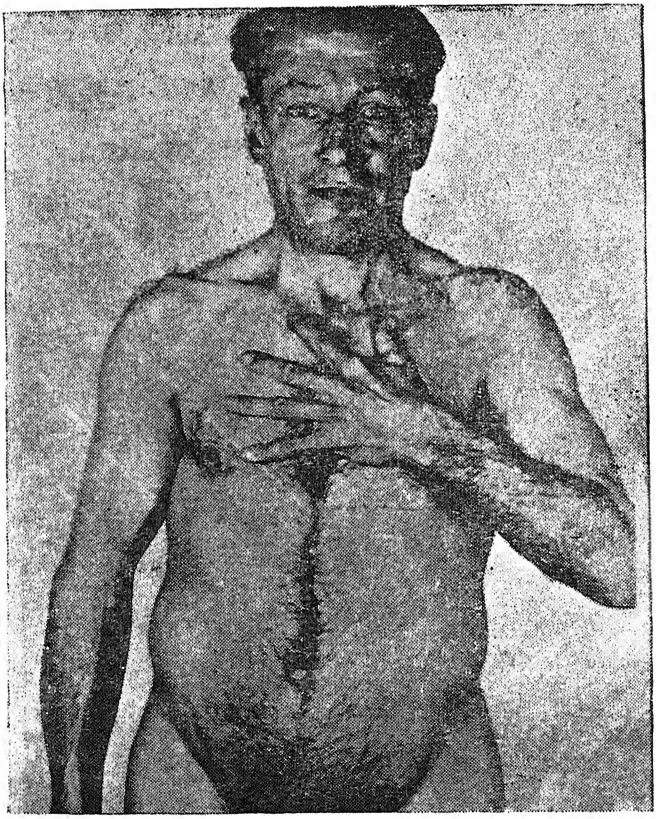


Figure 10

Dr. Prill often found dystrophic fibres scattered among normal fibres. The EMG of the extensors of the forearm (fig. 12) often shows dystrophic potentials, considerable phase abbreviation and lower amplitude potentials without increasing of interference density. In most cases stimulation with frequencies up to 50 seconds caused a noticeable diminution of the amplitude of the action potentials within the first seconds of the stimulation, and this in proportion to the frequency of the stimulation. Dr. Prill has performed the electromyographical examinations of the patients.

But all these findings seem to be unspecific, that means, they can be found sporadically and in a minor degree also in

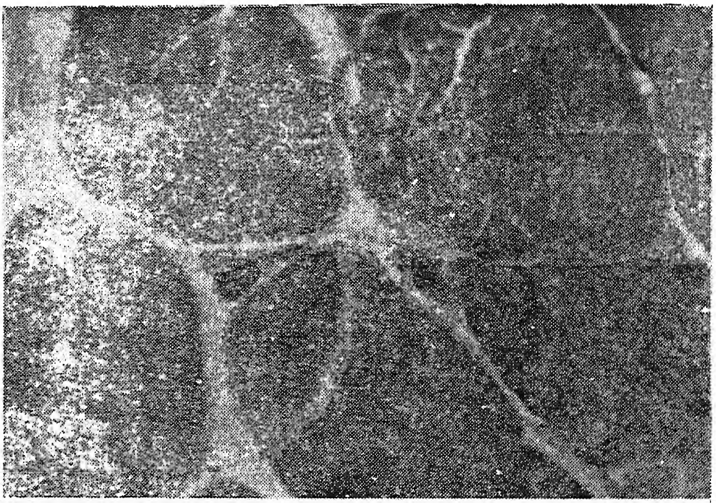


Figure 11

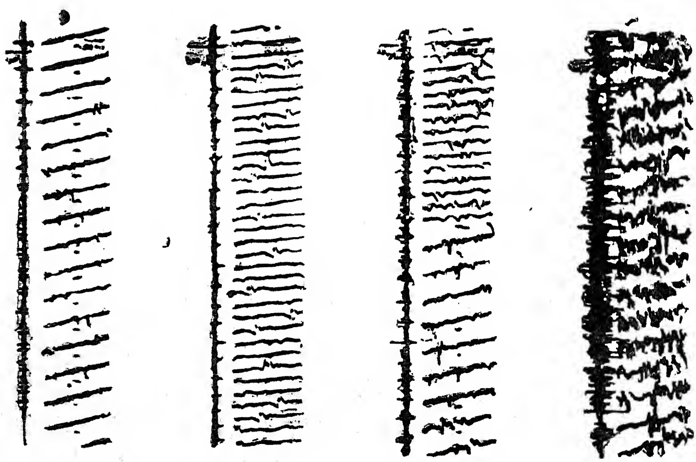


Figure 12

cases of Thomsen's disease, as far as I see. Otherwise the symptoms just mentioned are typical for the Recessive

generalized myotonia. This applies mainly in the male, in females recessive myotonia usually appears in a milder form than it does in males.

85 of the 97 propositi of the recessive type are males and only 12 females. The higher frequency of the male sex is easily to explain by a selection with respect to the degree of severity. It is interesting, that among the 55 affected siblings of the propositi, the so-called secondary cases, the ratio is 31 males to 24 females, which is not so far away from a balanced sex ratio.

Recessive generalized myotonia is more common than the dominant Thomsen's disease. For instance, the three patients described by Wilhelm ERB in 1886 in his well-known monograph "Die Thomsen' sche Krankheit" are not cases of real Thomsen's disease but of the recessive type. One of them was born in a small south-western German town, where one of my patients with recessive myotonia also comes from. Presumably both are distantly related as the same names occur in the ancestors of both pedigrees.

The next figure 13 shows the birth places of the 97 propositi of the recessive type. The birth places of the propositi of the other 16 families with sporadic or sibling cases in which a dominant transmission may also be possible are marked by a circle on the map. The geographical distribution is not yet analysed. But, as you see, families with recessive myotonia are spread over the whole Federal Republic. There are some loose accumulations of many or few cases in some districts, but the varying population density must be taken into consideration. it seems, however, that two or more families live in nearer neighbourhood more often than can be expected at random distribution.

Apparently the families which came to my knowledge and which are pointed out on the map are only a small proportion of the actual number of affected families in the Federal Republic. During the investigation it was found that persons suffering from myotonia often try to conceal their ailment. Most of them have experienced that they were regarded as simulants. This fact, along with shame, caused many to keep their ailment a secret even from close relatives. Many of the affected whom I

encountered through the family investigations never had consulted a physician. Generally the myotonia is not mentioned when medical help is sought for some other difficulty.

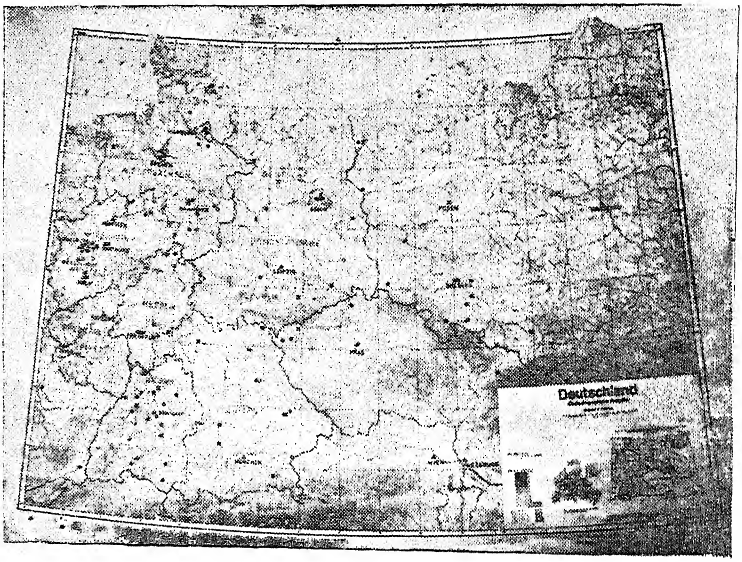
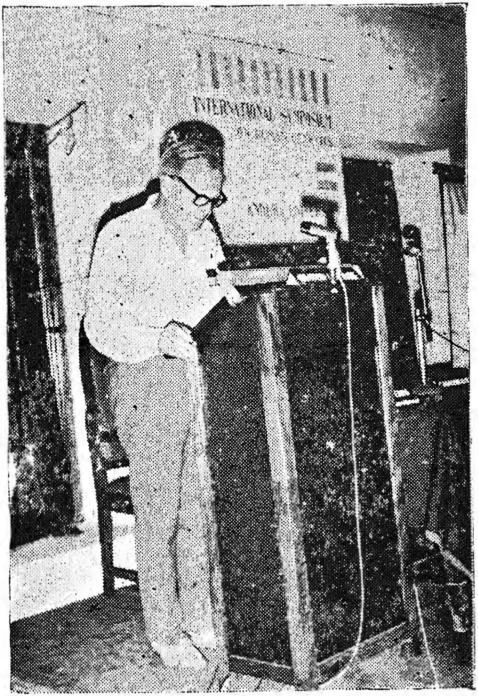


Figure 13

It may be assumed that a large number of affected persons in Germany thus never have come to medical knowledge. An approximate idea of the scale can be gained by estimation of the gene frequency with the aid of the frequency factor of first cousin marriages. If one assumes that the factor of 5% for first cousin marriages is correct and that this factor amounts to 0.5% for the general population, one could estimate that recessive myotonia would have a frequency of 36 per million. This means that there would be more than 2,000 persons affected with myotonia of the recessive type in the Federal Republic and Berlin, whereas I have found only about 135 patients.

Laboratory investigations have not been able to demonstrate any significant biochemical abnormality. In general the basic defect of a recessive disease is an enzyme defect, but in recessive myotonia this is not yet known. Therefore one cannot seek yet for a biochemical manifestation of the heterozygous



Prof. Dr. P. E. Becker, delivering the
Invited Lecture

state. A clinical manifestation of the heterozygotes could not be found.

Recessive generalized myotonia is an independent genetic type different from Thomsen's disease, Myotonic dystrophy and Paramyotonia congenita. In these three last mentioned types the transmission is dominant.

Paramyotonia congenita was at first described by Eulenburg. In the original family from Rostock seven generations with affected persons are known (fig. 14). I could find out a person belonging to this family which gave some information about

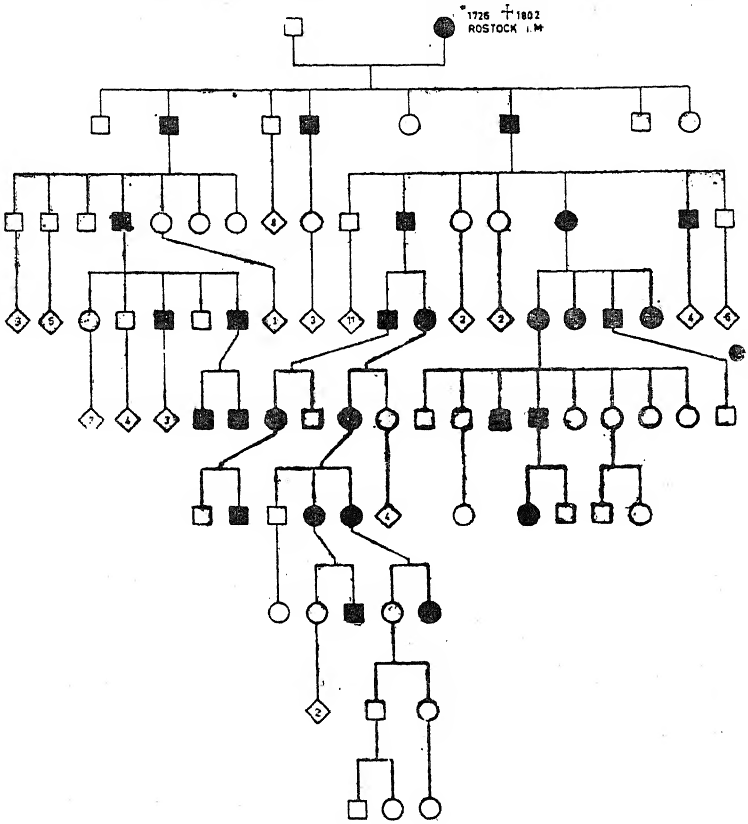


Figure 14

her affected relatives. In the two younger generations no affected persons are known.

Besides the six propositi obtained by the inquiry of neurologists and internists three further cases of Paramyotonia came to my knowledge through colleagues in the last years. Moreover, I was able to find a family published by Alsberg in 1898 near Bielefeld in Westphalia. Through this family I learned to know eleven further families in the Ravensberger Land. Thanks to a family doctor of a propositus in Hessen, discovered by the inquiry, I was able to add another propositus. Finally I found the patient published by Lewandowsky (1916). In this way 23 propositi were collected unsystematically.

In their families 308 persons affected from paramyotonia are known, 164 were alive, 157 of these could be examined.

Paramyotonia is transmitted regularly through several generations as the next figure 15 demonstrates. Among the children of affected persons 46±2, 3% also have paramyotonia and 54±2, 3% are healthy (with omission of the sibship of propositi). These numbers are in good agreement with the expected ratio of 1 : 1 in autosomal dominant transmission.

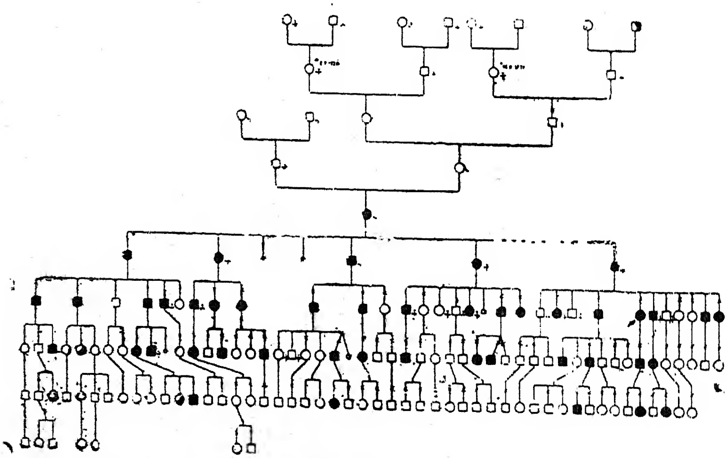


Figure 15

As you know Paramyotonia is congenital. When exposed to cold facial muscles become rigid (fig. 16) tonic contraction occurs, relaxing only in warmth usually within a few minutes. The hands become "clumsy" in the cold; the fingers are flected and abduced due to the tonic contraction of the intrinsic muscles

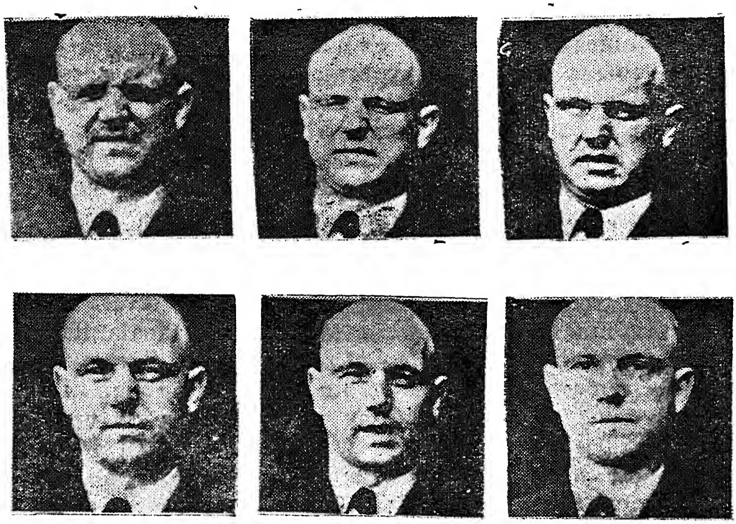


Figure 16

Abb. 12: Nach intensiver Abkuhlung des Gesichts fur 3 Min. wurde der Patient aufgefordert, die Augen kraftig zu schlie Ben. Die paramyotonische Kontraktion der mimischen Muskeln hat sich erst nach 8–10 Min. wieder ganz gelost (Die Aufnahmen verdanke ich Herrn Dr. Bohlen)

of the hand and perhaps of the muscles of the forearm (fig. 17). After a short time the stiffness of hands passes over to weakness and paralysis, which gradually r e s t i t u t e s in warmth within half an hour to several hours. The legs are less affected and their stiffness is not so impressive. After sitting or standing for a longer time in cold, the leg muscles may stiffen too, but stiffness mainly occurs only momentarily and weakness or paralysis of the legs is rare.

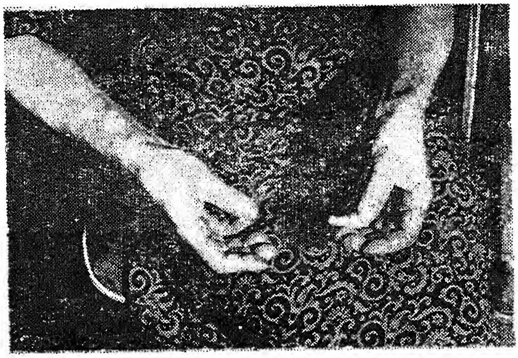


Figure 17

After severe cooling other muscles may occasionally become paramyotonic too; some patients indicated, every arbitrary muscle to be able to react paramyotonically by adequate cooling. Three patients had sporadically experienced generalized weakness similar to periodic paralysis with participation of the limb and trunk muscles. Besides these severely affected persons in other cases the manifestation is minor, only some facial muscles, specially the orbicularis oculi or those of the chin, become rigid by severe cooling: The eye-slits are slightly narrowed and the chinskin is wrinkled, while the limbs are completely free, or only the hands are weak by severe cooling for a few minutes. There are considerable individual differences of susceptibility and extension of paramyotonia. Paramyotonia generally remains unchanged from birth on through life; It may become more severe during pregnancy, so that the leg muscles stiffen even in warmth, but this is transitory. Hypothyroidism also causes generalisation of paramyotonia and impairment of muscles stiffness and weakness, so that all movements are severely hampered, independent of cooling. In such a case treatment with thyroid hormone is successful.

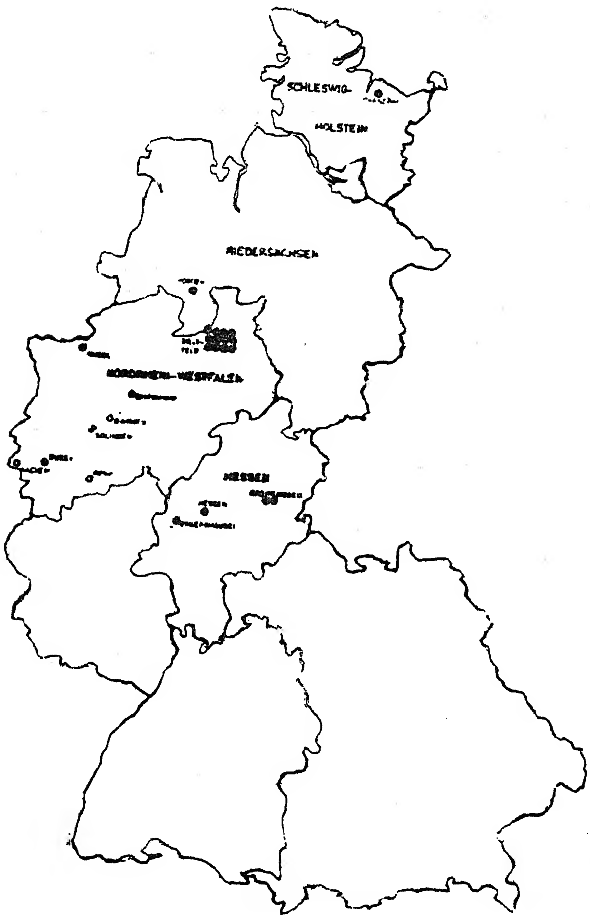
Laboratory investigations have not been able to demonstrate any significant abnormality. The potassium level in blood serum is normal. In some cases potassium intake may lead to an increase of myotonic signs and paramyotonic symptoms. On the other hand generalized weakness seems, if at all, to be connected with lowered serum potassium level. But the results are inconstant, a certain lability of the potassium level in some paramyotonic persons seems to be characteristic.

Both sexes are almost equally often affected. In my material there are 160 males and 147 females, that means $52 \pm 2{,}9\%$ to $48 \pm 2{,}9\%$. But the sexes differ in the degree of severity; in females paramyotonia appears usually in a milder form than it does in males.

The paramyotonic susceptibility shows a wide variation in both sexes. In the degree of severity siblings resemble each other much more than may be expected by chance; on the other hand, parents and children do not resemble each other more than incidentally. In other words: The sib-correlation in respect to the degree of severity is relatively high, namely $r = 0{,}6 \pm 0{,}09$ and a parent-child correlation does not exist ($r = 0{,}15 \pm 1{,}3$). This phenomenon may be explained according to Penrose: The abnormal gene depends on its expression

upon its "normal allele". This exists in different forms in the population, a polymorphism is reasonable.

The distribution of paramyotonia in the Federal Republic has some interesting aspects of population genetics: On the next figure the residences of the eldest known paramyotonic patient of each family are pointed out on the map (Fig. 18).



Map of the German Federal Republic

- • Birthplaces of the eldest known affected members of the 23 families with Paramyotonia congenita
- o Birthplaces of the eldest known affected members in the families reported by HOLLMANN (Barmen) and HUBNER (Bonn)

Figure 18

I succeeded in ascertaining genealogical relations between several families of the 23 propositi, thus finally 18 kinships showing 308 cases of paramyotonia could be established. Obviously all affected persons, living near Bielefeld in the Ravensberger Land as well as the one from Dortmund and the one from Vörden, originate in one and the same mutant. One may assume that this is also the case for the paramyotonic patients in the Western part of North-Rhine-Westphalia as well as for those in Hesse. Let me mention that all cases of Paramyotonia ever published in the geographical area of the German Federal Republic are either propositi of my investigation (Alsberg 1898, Lewandowsky 1916, Böhlen 1948) or could later be indentified as members of the investigated families (Funcke 1898, Schott 1936, Wawersik 1947, Ostheidehuster 1947), with the exception of two cases, one described by Hollmann (1894) in Barmen, the other by Hubner (1917) in Bonn, which I could not find. They are marked by a circle on the map. Thus outside of a relatively small region in the middle of the Federal Republic no cases of paramyotonia are known. Therefore one could assume, that all known affected persons in the German Federal Republic originate in one and the same mutant occurring before the second half of the seventeenth century. The only exception is the sporadic propositus in Schleswig-Holstein representing a new mutant. One may assume that the older mutant originated in the Ravensberger Land. This is supported by the remarkable accumulation of cases in this area, where paramyotonia in several families can be traced back through many generations. In addition the ancestors of at least two other families, who have been residing outside the area for several generations are known to stem from the Ravensberger Land.

Paramyotonia congenita (Eulenburg) is a pure myopathy. It differs from Thomsen's disease among others by an impressive dependency upon cooling, by the subsequent "cold paresis" and by a different myotonic behavior: While in Thomsen's Myotonia congenita the myotonic contraction disappears gradually after repeated muscle action, in Eulenburg's disease, on the contrary, the stiffness aggravates with repeated action, which has been called "Paradoxical myotonia".

Many authors suggest that Paramyotonia congenita and

Adynamia episodica hereditaria (Gamstorp) or Hyperkalemic periodic paralysis may be identical conditions. This is an erroneous supposition, which has its origin in the existence of another genetic type, different from Paramyotonia congenita as well as from Hyperkalemic periodic paralysis. This type has in symptomatological respect a midposition between both types above mentioned. It is characterized by the symptomatological combination of paramyotonic behavior occurring not only in the cold but also at warm temperature. In addition one observes long lasting attacks of weakness with onset mostly during the night or early in the morning and independent of exposure to the cold. I should like to name this type "Paralysis periodica paramyotonica". In this type potassium intake leads to attacks of paresis or paralysis, while in Eulenburg's Paramyotonia potassium aggravates paramyotonic stiffness at least in some cases, but causes no weakness. I observed two families of this type, one with four the other with severe affected persons. One family lives in the southern, the other in the Northern Germany. Both stem from Landberg a.d. Warthe, now in Poland. Transmission is dominant.

To come to the conclusion: Most cases which have been diagnosed as Thomsen's disease are actually those of the recessive type of generalized myotonia. Recessive generalized myotonia and dominant Thomsen's disease are two different genetic entities. The gene responsible for the defect is not yet known neither in the recessive nor in the dominant type. Most probably it is different in both types. Recessive diseases are in general based on an enzyme defect and dominant diseases mostly on structural abnormalities of cells or tissues (Lenz). In future it will be an important task to discover the different basic defects.

Both diseases are much more frequent than is generally supposed. Thomsen's disease shows a wide variability in its expression. Slight manifestations seem to be more often than severe expressions. Only the latter cases come to medical knowledge and of them only a small proportion. In Recessive generalized myotonia the myotonic disease is in general much more severe than in Thomsen's disease.

Paramyotonia congenita is different from Thomsen's disease. The degree of severity is variable in Paramyotonia congenita depending upon the "normal" allele. There are some indications that all or nearly all known affected persons in the Federal Republic originate in one and the same mutant. Paramyotonia congenita is different from Periodic paralysis with myotonia or from Paralysis periodica paramyotonica. Besides Myotonic dystrophy and the afore mentioned types some rarer myototic types exist about which little is known until now.

SERUM ALKALINE PHOSPHATASE IN KUMAON REGION (NORTH INDIA)*

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When serum or plasma alkaline phosphates is subjected to electrophoresis, two phenotypes are observed upon suitable histochemical staining. Arfors et al (1963) have classified them as Pp1 showing only a fast-moving zone A and the other as Pp2 where a slow moving band B is also present. Band A is present in all individuals while band B is variable. On the basis of Twins and Family material Arfors et al (1963) have suggested that band B is under genetic control. Shreffler's (1965) study of twins could not demonstrate the complete concordance in case of Monozygotic twins. The observed variations was attributed to temporary causes and technical errors. From the studies of Arfors et al (1963), Bamford et al (1965), Beckman (1964), Shreffler (1965) and Walter (1967, 1970), we know that the presence of band B is affected by other genetic systems like ABO blood groups and ABH secretion etc. as well as by environmental factors like nutrition and age. Walter (1968) noted considerable variation in the frequency of band B among different populations. No doubt it is complicated to interpret the variation, as to whether it is due to genetic or non-genetic factors. To enhance our knowledge in this respect we have to study further different populations of different genetic background and different environmental conditions. Keeping this in mind, four endogamous groups (Brahamins, Rajputs, Doms and Tharus) from Kumaon region (North India) were studied for serum alkaline phosphatase.

*Supported by the Deutsche Forschungsgemeinschaft.

Material and Methods

The present material was collected during a population genetic survey (1968–69) of Kumaon region. Only male individuals between the age group 18–60 years are included in the sample. The sample consists of 104 Brahmins, 130 Rajputs, 80 Doms and 152 Tharus.

The material is analysed according to the Arfors-method as described by Walter et al (1967).

Results and Discussions

Table 1 shows the distribution of Pp2 in the four investigated groups. Pp++ and Pp+ are added together and treated as Pp2. No significant differences are to be observed in the distribution. Chi-square test confirms the homogeneity of Pp2 among the four populations? The range of variation is between 26.15% for Rajputs to 32.89% for Tharus.

Table 1

Distribution of Alkaline Serum Phosphatase

Population	N	Ppl	%	Pp2	%
Brahmins	104	72	(69, 23)	32	(30, 77)
Rajputs	130	96	(73, 85)	34	(26, 15)
Doms	80	57	(71, 25)	23	(28, 75)
Tharus	152	102	(67, 11)	50	(32, 89)
	$\chi_3^2 = 1, 61$; $70 > P > 50$				

Walter (1970) has shown, that individuals before puberty possess a low frequency of Pp2 types than the group after. Since the present material contains individuals of more than 18 years of age, the age factor does not seem to contribute to the observed variability. Variation due to technical errors has to be excluded as the collection and analysis of material has taken place under similar conditions. At present we can only say that the observed differences between the groups seem to be due to chance.

Table 2 shows the distribution of Pp2 in A, B and O blood group individuals. Due to a small number of individuals observed, A B blood group is omitted. The first glance at the table confirms the expected association of Pp2 with B and O individuals in all the four groups. Number of A individuals possessing Pp2 is small. The distribution of Pp2 in B and O individuals in the four groups is homogeneous. In other words we can say that the degree of association between Pp2 and A B O

TABLE 2

Alkaline Serum Phosphatase and ABO Blood Groups Distribution

No.	Population	N	Pp1	%	Pp2	%	ABO Blood Groups
1.	Brahmins	40	25		15	37, 50	0
2.	Rajputs	40	26		14	35, 0	
3.	Doms	22	12		10	45, 45	$\chi_3^2=1,204$
4.	Tharus	33	18		15	45, 45	$80>P>70$
1.	Brahmins	31	18		13	41, 93	B
2.	Rajputs	35	20		15	42, 86	
3.	Doms	26	15		11	42, 31	$\chi_3^2=0,243$
4.	Tharus	67	36		31	46, 27	$97,5>P>95$
1.	Brahmins	25	21		4	16, 00	A
2.	Rajputs	47	43		4	8, 50	
3.	Doms	26	25		1	3, 80	—
4.	Tharus	32	31		1	3, 12	—

blood groups is the same in the four endogamous groups. Chi-square test could not be applied in case of individuals as the number is small. All the groups show a low frequency of Pp2. It varies from 16.0% in case of Brahmins to 3.13% for Tharus. These differences may be due to a small sample size. The trend remains the same that frequency of Pp2 is low in A individuals.

For the purpose of comparison of the Pp2 distribution, populations belonging to different geographical areas and ethnic

background are presented in Table 3. To keep the methodological error to the minimum only those populations which were analysed in the Institute of Anthropology, Mainz are included. In this table, the four endogamous groups of Kumaon region are treated as one complex as no differences were found in the distribution of Pp2. All the populations represented here are

TABLE 3-a

Distributiou of Serum Alkaline Phosphatase in Various Populations

No.	Population	N	Pp1	%	Pp2	%	Author
1.	Angola	899	826	91, 88	73	8, 12	Walter (unpublished
2.	Crete Island (Greece)	195	168	86, 2	27	13, 8	Walter (1968)
3.	Germans	170	129	76, 0	41	24, 0	,,
4.	Greeks	220	153	69, 55	67	30, 45	,,
5.	Hungarians	162	120	74, 0	42	26	,,
6.	Icelander	115	41	35, 6	74	64, 4	,,
7.	Indians (Kumaon)	466	327	70, 17	139	29, 83	Present study
8.	Iranians	363	245	67, 5	118	32, 5	Walter (1968)

TABLE 3-b

Comparison of Serum Alkaline Phosphatase

No.	Population	χ^2	P
1.	All the eight populations	270,93	P<0, 1%
2.	Without Icelander, Crete Island and Angola	5,05	30>P>20
3.	Angola+Crete Island	6,37	2,5>P>1

male individuals. The distribution of Pp2 in the given populations show significant differences. The frequency varies from

8.12% (Angola) to 64.4% (Icelanders). The distribution of Pp2 shows homogeneity among Germans, Hungarians, Greeks, Iranians and Indians (Kumaon). The low frequency of Pp2 among the Greek population of Crete island is difficult to explain. Langman et al (1966) have shown the effect of fat consumption on intestinal alkaline phosphatase of individuals belonging to a particular genetic structure (B and O Secretors). Walter (1968) suggested that the high frequency of Pp2 among Icelanders may be due to high rate of fat consumption when compared with other European populations. However, on the basis of our present material we could not observe a trend where different dietary habits may contribute to the variability of Pp2 distribution. Though we do not have data on the food habits of the investigated populations, but we know that the fat consumption of Iranians and Indians (Kumaon) is not the same as Germans or other European populations. Under the influence of diet we should expect lower frequency of Pp2 among Asian populations. But this is not the case. This only points to the complications involved in interpreting the variability observed in the distribution of Pp2. So far no other African population except from Angola has been investigated. Therefore it is difficult to say whether the lowest observed frequency of Pp2 is due to the local effects or characteristic of population inhabiting this region.

Summary

The distribution of serum alkaline phosphatase has been studied for four endogamous groups (Brahmins, Rajputs, Doms and Tharus) from Kumaon region, North India. The intergroup differences are not-significant. The range of variation of Pp2 is between 26.15% for Rajputs to 32.89% for Tharus. The four endogamous groups investigated here are similar to Germans, Hungarians and Greek as far as the distribution of Pp2 is concerned.

Acknowledgement

I wish to expresss my thanks to Prof. H. Walter, Institute of Anthropology, University of Mainz, for giving me his unpublished data.

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THE GENETICS OF ATHEROSCLEROTIC HEART DISEASE AND LIPID DISORDERS

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Diseases with multifactorial genetic background are more difficult to investigate than rare diseases with Mendelian inheritance. However, to many this group of diseases poses the greatest challenge and this even more so, since it preferentially comprises common diseases of great epidemiological and medical importance. Studies of geographic, social and ethnic differences in distribution may offer important contributions to our understanding of the interplay of environmental and genetic factors in these diseases. As an example I like to discuss atherosclerotic heart disease and related lipid disorders.

During the last decades an alarming increase of atherosclerotic heart disease has been noted in most Western industrialized nations. This certainly must be the consequence of external factors, because the time span involved is much too short to permit a change in gene frequency of the required magnitude under any genetic hypothesis. Nevertheless, even under the same environmental conditions only a fraction of about 5% of men become affected by clinically manifest coronary artery disease at an early age, and the severity of morphologically seen involvement, present in many more, shows great variance. We, therefore, may ask, whether the manifestation of coronary artery disease depends on genetic factors, whether there are genotypes that confer a specific risk and whether the knowledge of such genetically determined liability may offer a chance to employ preventive measures.

Genetic determination and susceptibility to environmental influence are not mutually exclusive. Their strong interaction is rather the rule in common diseases with a definite hereditary

background. To stress this point, I may remind you that only very few if any hereditary diseases are independent of environment and that probably very few of the environmental diseases are not influenced by the genotype of the patient. Think of the influence of diet on Phenylketonuria or Galactosemia and of the influence of certain genotypes on the consequences of malaria infection or the influence of bloodgroups on the course of small pox. Diabetes is another example of strong influence of diet factors as well as genotype. This last disease is a good example for the common diseases to be placed in the mid-area of our scheme.

Let me start the discussion of my special subject by stating the hypothesis, that atherosclerotic heart disease belongs to the group of diseases with a multifactorial genetic basis, being strongly influenced in its manifestation by exogenous factors and let me briefly summarize the evidence for this statement.

It is an age old clinical impression that early coronary heart disease runs in families. A number of newer anamnestic studies has confirmed this. Again and again has the disease been shown to be more common in sibs or parents of patients than in matched controls. This held true for relatives of both sexes and it was confirmed also by epidemiological studies of entire communities as in the Tecumseh-Study conducted by Epstein and Co-workers. These findings cannot be taken as evidence for genetic factors without reservation.

Even if a bias by underreporting among relatives of controls is excluded, as for example in the community study of Epstein common dietary factors among relatives cannot be ruled out. There are two ways out of the dilemma : twin studies and detailed analysis of family data by special methods. There are several impressive studies of single monozygous twin pairs with closely concordant disease-history and findings. Detailed clinical observation on twins may give evidence of similarity in the course of disease and may reveal special contributing factors, particularly if pairs are studied which appeared discordant for some time and under variant environments. Much greater weight for the general question carry of course

unselected twin series. These are rare. Table I summarizes two such studies. Whereas the series of Kahler and Weber appear to be small, it is based on personal examination. The large Danish series in contrast rests entirely on questionnaire data. This causes some uncertainty in regards to zygosity as well as to clinical diagnosis. Since only manifest infarction at a given date was counted, slight differences in time of manifestation could render twins discordant. The figures, therefore, represent a minimum estimate and probably are too low.

TABLE 1

Myocardial Infarction in Twins

Authors	MZ Conc.	MZ Disc.	MZ Conc. Rate	DZ Conc.	DZ Disc.	DZ Conc. Rate
Kahler and Weber, 1939	6	2	0,75	4	22	0,15
Hauge et al, 1968	40	82	0,33	48	131	0,27

Figure 1 is taken from an other study with a similar approach on about 6000 twins in Sweden, studied by Cederlöf by means of a special questionnaire, recommended by the WHO for epidemiological use. In both age groups studied, monozygous twins appeared in a much higher proportion concordant than dizygous twins.

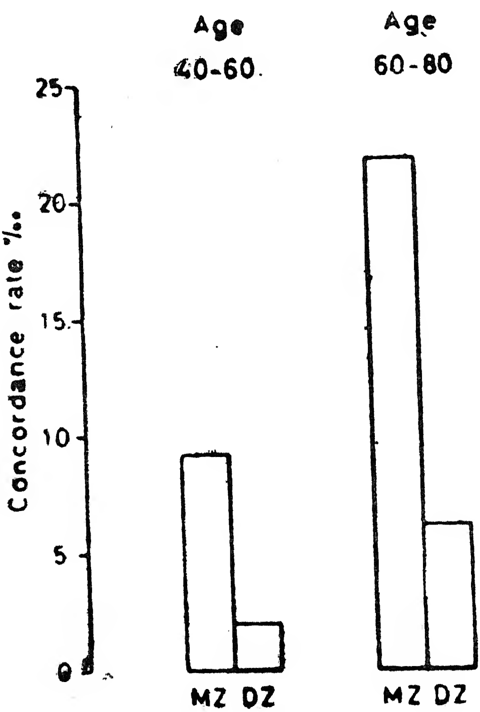

Figure 1

Concordance rates for angina pectoris by age and zygosity according to Cederlof et al, 1967. MZ indicates monozygosity, DZ dizygosity.

Of Special interest in regards to the possible mode of inheritance are studies analyzing internal characteristics of family data. As an indicator may be used the risk to children according to mating types of parents.

A trait, which to a significant extent is determined by multifactorial inheritance, should show a decreasing proportion of affected children in families with both, one, or neither of the parents affected. Such evidence has been presented by Thomas and Cohen, Thomas and Ross and using the same material by MURPHY 1965 (Table 2). These studies have been criticized on various grounds, the risk differential quoted here, however, appears to be real.

TABLE 2

Family Data on Coronary Disease
(Data of Thomas and Cohen, 1955 and Murphy, 1967)

Parents (Grandparents of index person)		Children (Parents of Index Person)					
		Sons			Daughters		
			Positive			Positive	
Father	Mother	Total	n	%	Total	n	%
—	—	414	(17)	4,1	380	(10)	3,4
±	∓	184	(15)	8,2	207	(5)	2,4
+	+	63	(11)	21,2	49	(2)	4,1

Within a joint study of nine German university hospitals, primarily aimed at therapeutic problems, we also could collect family data. Anamnestic data on the incidence of infarction among sibs of probands confirmed the same pattern reported by the earlier authors (Table 3). This conforms to expectation, if multifactorial inheritance is assumed.

TABLE 3

Family Data on Myocardial Infarction

	Parents		Sibs of Probands			
				Positive		
	Father	Mother	Total	n	%	χ^2 (against A)
A	—	—	1943	(54)	2,77	
B	±	∓	232	(24)	10,3	p<0,001
C	+	+	20	(3)	15,0	p<0,001

Fuhrmann and Oberhoffer
(unpublished)

Even stronger support for the hypothesis of a multifactorial genetic basis comes from a separate analysis of incidences in relatives according to the sex of probands. This argument has been first advanced by Carter for Pyloric stenosis. The reasoning is as follows: Let us assume a disease, and in our case coronary heart disease, being determined by a genetic liability and showing unimodal distribution in the population. Beyond a certain threshold the likelihood of manifestation may rise steeply. In any disorder, genetically determined in such a way and preferentially manifested in one sex, one may assume that members of the less susceptible sex are protected by sex specific factors. In order to manifest the disease in spite of these sex dependant characteristics they must have a higher "dose" of the disease favouring genes: In the mean they are taken from the further right and of our distribution (Figure 2). Since close relatives have a fixed percentage of genes in common, relatives of such patients in the average also must have a higher number of these genes than same-degree relatives of index, patients belonging to the susceptible sex. If this type of reasoning is applied to coronary heart disease, a higher proportion of affected individuals should be found among close relatives of affected women, than among the same group of relatives of affected men. This has been studied by Slack and Evans 1996. Comparing adult first degree relatives of 121 men and of 96 women with ischaemic disease and 104 men and 105 women controls the following results were obtained:

"When deaths under 55 years in men and 65 years in women are considered, the relatives of both sexes of female patients with onset under 65 years show a nearly 7-fold increase compared with general population and the male relatives of the male patients with onset under 55 years show an increase of risk of death, which is five times that in the general population. The female relatives of the male patients experience an increased risk which is 2 1/2 times that of the women in the general population." This differential increase in risk of early death from ischaemic heart disease is even more pronounced in first degree relatives of patients with hypercholesterolaemic xanthomatosis. The increase is 12 to 13 times in "younger" first degree relatives of males and 25 times in the same group

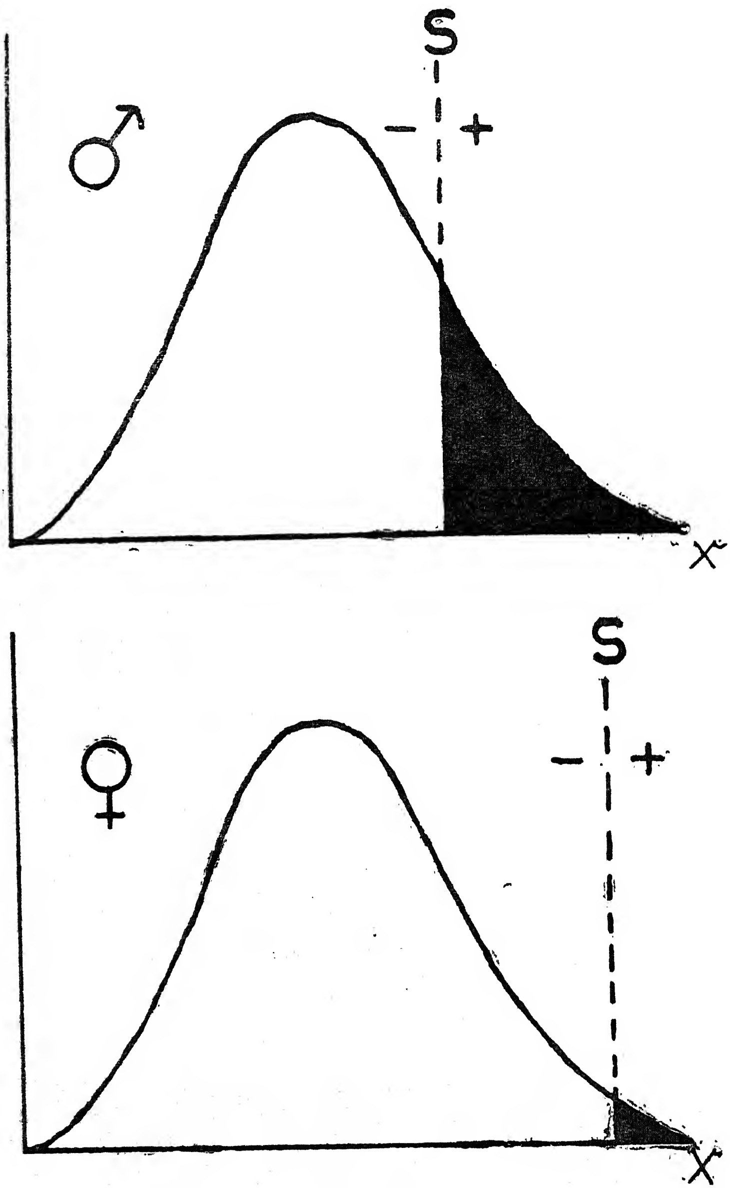

Figure 2
Distribution of affected individuals (black) among the population. Assumed is a disease with multifactorial genetic background and considerable higher incidence in males (see text). χ = genetic predisposition
S = threshold

of relatives of female index patients (Slack and Nevin, 1968) (younger here means below 55 years in men and below 65 in women).

We used the material of the previously mentioned joint study in Germany for a similar analysis and compared the incidence of infarction in sibs of male and female probands (Table 4). In all subgroups was the difference in the predicted direction, and for the total it proved to be statistically significant at the 5% level. This estimate will be improved, if the probands are grouped according to age. It is difficult to account for this risk differential in any other way than by multifactorial inheritance.

TABLE 4

Infarction in Sibs of Probands

Sex of Probands	Sibs Total	Positive n	Positive %	χ^2
♂	2635	(91)	3,45	$p<0{,}05$
♀	800	(40)	5,0	

Fuhrmann and Oberhoffer (unpublished)

The conclusion, that besides of environmental factors multifactorial inheritance is of considerable importance in coronary heart disease, immediately leads to the question, whether it is possible to identify an association of the manifestation of this disease with other variables of known inheritance.

Commonly used markers are blood groups, which follow simple Mendelian inheritance. A disease incidence significantly different for persons possessing various bloodgroups, therefore, constitutes one of the clearest examples of genetically determined diathesis in disease. The same holds true for other simply inherited polymorphisms. For ischaemic heart disease

the matter of bloodgroup association has been controversial, but a recent combined analysis of 12 independent series comprising 2763 patients and 218 727 controls (by Vogel and Krüger) revealed a highly significantly greater incidence among persons of bloodgroups A than among those of bloodgroup O (p 0.0027). Patients of bloodgroup A were 1.18 times more often affected than those of bloodgroup O. In the same order were the differences between bloodgroups B and A B versus O, although the level of significance was lower due to the smaller numbers (between p 0.01 and p 0.05). For the combined groups of A, B, and AB versus O the result resembled closely the figures given for A versus O at the same high level of significance. The biochemical basis of this association is unknown, but a certain clue may be seen in the results of various authors in Greece, Scottland, England and Thailand who confirmed a positive correlation of bloodgroup A and higher concentration of cholesterol in the serum. In a cooperative study in England and U.S.A. by Jick and co-workers it could be shown that among women taking oral contraceptives thrombembolism occurred more frequently in those of not–O blood groups than in women of blood group O.

There are apparently close links between atherosclerosis and infarction on one side and disorders of lipid metabolism on the other. In spite of a great number of studies the general problems are far from being solved. Of great interest are, therefore, the clinically and genetically better defined hyperlipidemias. During the last five years the classification proposed by Fredrickson and co-workers has been widely accepted (Fig.3).

Genetically best defined is hyperlipoproteinemia type I, which corresponds to the classical picture of exogenous or fat-induced hyperlipidaemia, first described by the Bürger and Grütz in 1932 in Germany. It is characterized by the presence of chylomicrons in plasma 16 hours after a normal meal. The serum is milky and on standing over night in the refrigerator a discrete cream layer will separate at the top. On electrophoresis the chylomicron fraction at the start is enlarged, all other lipoproteins appear rather low. The disease usually manifests in childhood with bouts of abdominal crises and occasional

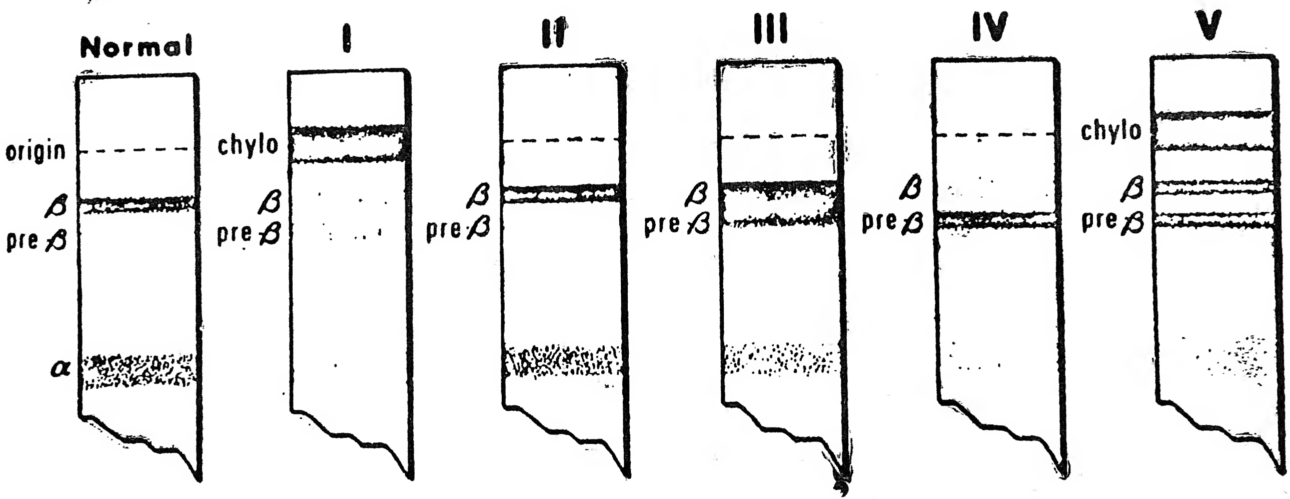

Figure 3

Schematic representation of five types of familial hyper-lipoproteinemias as defined by electrophoresis (after Roberts, Levy and Fredrickson, 1970).

eruptive papules. The disease is rare, only some 50 cases and only about half a dozen family studies have been reported. It appears to be autosomal-recessively inherited, the basic defect being a deficiency of a postheparin lipolytic enzyme involved in the breakdown of chylomicrons. It is remarkable, that in spite of the markedly elevated triglycerides no increased risk to atherosclerosis has been found.

From this aspect the hyperlipoproteinemias type II, III and IV deserve greatest interest. All three are commonly associated with severe early atherosclerosis. Longest known is type II, familial hypercholesterolemia, it is also a rather common type. In the typical case cholesterol is high, triglycerides are normal and the serum thus appears clear. Electrophoretically beta-lipoproteins are elevated. This pattern may be secondary to other disease, but also may be familial due to a single autosomal gene which is dominant or incompletely dominant. Patients may show spectacular narrowing of coronary arteries, and in homozygotes this may occur in youth or even childhood. An apparent clinical sign may be a corneal arcus in a child. In severe or long standing disease tuberous and tendon xanthoma appear. Treatment of type II is difficult and not very successful.

Only recently has a sub-type been recognized, in which in addition to cholesterol triglycerides are moderately elevated. This is called type IIa by Fredrickson and type II plus IV by Kuo. Type IIa can easily be confused with type III unless electrophoresis and ultracentrifugation are employed. Thus a family seen by us earlier probably represents this type, but could possibly also belong to type III. This type also does not respond too well to therapy.

This is quite different in hyperlipoproteinemia type III, which probably is not as rare as has been thought and which responds well to treatment. This type originally has been described by Fredrickson as broad beta disease, according to its typical pattern in lipid electrophoresis. It also is a familial disease and comprises hypercholesterolemia plus hypertriglyceridemia of various degree. Both fractions commonly are between 400 and 800 mg. per 100 ml., but typical patterns may be observed at much lower levels. The plasma thus may be clear, cloudy or milky, commonly with a yellowish stain. The

lipid-burdened beta-lipoprotein is abnormal in composition and density. On electrophoresis thus a broad beta band appears, after ultracentrifugation (16 hrs. 100.000 g.) most of the lipoprotein with beta mobility is found in the fraction with density of less than 1.006 (floating beta), whereas in the other types the lipoproteins with beta mobility appear in the infranatant (density greater than 1.006).

Seidel (1970) could prepare an antiserum that precipitates the floating-beta-lipoprotein of type III patients. This would prove, that an immunologically altered protein is involved. At present, however, results are still inconsistent and it is not yet clear, to what extent this test is influenced by quantitative phenomena.

Clinically patients may show tuberous xanthomata at the preferential sides of the elbows, knees and buttocks. Most characteristical, however, when present, are orange-yellowish xanthomata at the palms of the hands and the creases of fingers, toes and breasts. They are not seen in this form in other hyperlipoproteinemias. Type III has been considered to be quite rare, but a search among the patients of our medical clinics and referrals from nearby hospitals led us to doubt this. No detailed family reports have been available so far. Vertical transmission has been mentioned by Fredrickson and co-workers, but as they state, the genetics have remained unclear. It has been suggested by Roberts and co-workers, that patients represent homozygotes, and some genetic relationship to the more common type IV has been suggested in another paper. A very large pedigree that we could observe, permits to examine this. Only the index case had gross hyperlipoproteinemia before treatment, several others, however, showed moderate elevation of lipids and typical patterns in the lipid-electrophoresis. Patterns of type III have been found after ultracentrifugation and in some members of the family were confirmed immunologically by Seidal. From the data available so far, it rather seems that an autosomal gene in single dose may govern the development of lipoprotein pattern of type III. Manifestation seems to vary individually and also be influenced by age.

Very rarely only has the pattern been described in a child.

The reason for this of course may be, that the disease usually is not expected and not searched for in the absence of clinical manifestation, which will appear only later in life. Thus, the children in our pedigree seem to be the only patients of this age group on record with evidence of hyperlipoproteinemia type III.

The relationship between hyperlipoproteinemia type III and type IV in our pedigree remains unexplained. In view of the common occurrence of type IV in general it could be thought to be incidental. The seemingly unrelated spouses in this pedigree all stem from a small village and its neighbourhood with a high degree of intermarriage. Definite conclusions on the mode of inheritance of type III hyperlipoproteinemia will be possible only after further family studies are available. We have other families under observation, which seem to support the assumption of single gene inheritance with vertical transmission. The disease leads to early severe narrowing of coronary and peripheral arteries. From the scanty morphological reports availabe it appears that these are caused by a different type of atheromatous lesion as in type II or IV hyperlipoproteinemia. The lesion is dominated by foam cells and fibrous tissue and lacks pultaceous debris and cholesterol clefts. Calcific deposits are rarely seen and small. The important feature of this type of lesion is, that it apparently is able to regress, if the hyperlipoproteinemia is corrected. This is possible in type III by diet, by weight reduction and Clofibrate. A correct diagnosis, therefore, is important, and genetic analysis and guidance of the individuals at risk opens the way for an effective prophylactic regime.

The most common and genetically least clear hyperlipoproteinemia is type IV, also known as carbohydrate-induced hyperlipemia. It is characterized by an increase of the prebeta-fraction in lipid electrophoresis, which results from overproduction or defective clearance of endogenous glycerides from plasma. Triglycerides are elevated, cholesterol level is normal or moderately increased. The plasma may be clear, cloudy or milky. This pattern is frequently seen as a secondary feature due to other diseases, but it also is common as a primary disease. It occurs familial, but the transmission is unclear.

It has been suggested that type IV patients may represent heterozygotes of the same gene that causes type III when present in double dose. Little evidence has been produced for this assumption. It also could be discussed, that type III and type IV genes represent alleles at the same gene locus, other evidence suggests multifactorial inheritance of type IV. Family studies have been insufficient for definite conclusions, the admixture of secondary cases renders the analysis cumbersome.

Type IV lipoproteinemia is extremely common in patients with coronary heart disease. Recent studies suggest the presence of this pattern in little more than 50% of patients. Severe atherosclerosis has been found very early in patients with type IV hyperlipoproteinemia, deposits may be of the complicated type. Because of its frequency further genetic studies of this type of lipid disorder may contribute considerably to our understanding of coronary heart disease.

In type V finally chylomicrons and prebeta-lipoproteins are greatly elevated. It has been called mixed hyperlipemia, implying a mixture of features of type I and type IV. This designation, however, is awkward from a genetic point of view. The plasma is often yellowish and creamy, a top layer of chylomicrons separates after standing or centrifugation. This type is most frequently found secondary to other diseases (nephrosis, myxedema, diabetes, alcoholism, pancreatitis, glycogen storage disease etc.), but it also may occur as a primary inherited disease. The mode of transmission has not been worked out. Abdominal crises are frequent. Premature cardiovascular disease does not seem common.

Other established associations of coronary heart disease with genetically determined diseases concern diabetes mellitus and hypertension. Both themselves most probably follow multifactorial inheritance. Rather than to discuss this more closely, I like to turn to a more general aspect. If, as it appears to be, genetic factors contribute significantly to the incidence of coronary heart disease, responsible genes must occur with considerable frequency. While it certainly is true, that coronary heart disease mainly manifests after completion of the reproductive phase and thus selective pressure is lessened, the number of early death from such disease, that follows for

example in hyperlipidemias, should have diminished the frequency of these genes, unless they offered some other advantage under different circumstances. As for diabetes it has been suggested also for genes underlying atherosclerotic heart disease, such as for example genes involved in hyperlipidemias, that they might have been advantageous at times of scarce or irregular food supply. The recent increase in industrialized nations then might be explained in part by excess food supply rendering these genes deleterious. One, therefore, may look for comparison with populations, where this change has not yet taken place, or where parts of the population live under circumstances not yet affected by industrialization. Such a comparison could in the first place give information about exogenous factors involved in disease frequency. It also could give information about the influence of genetic factors, if genetically different populations or groups can be studied within the same environment. Very few studies have been available. I may mention the comparison of Asian and African components in the population of Uganda by Shaper and Jones, the comparison of the three racial groups in Cape Town (of Whites, Bantu and Cape colored) by Sacks (1960) and the autopsy study of Danaraj and coworkers (1959) on Chinese and Indians in Singapore. The latter authors found coronary heart disease among Indians in Singapore considerably more frequent than among Chinese in Singapore. They were convinced, this not to be an artefact and emphasized, that both groups were comparable in regards to environmental factors. This, of course, is very difficult to establish beyond doubt, even if both racial groups are living in the same area.

Differences in racially distinguished subpopulations in coronary heart disease have also been shown by Ashley in Wales in Great Britain, where individuals of Welsh origin appeared to be more prone to atherosclerotic heart disease and diabetes than the population at large.

In a study of Poon-King and co-workers in Trinidad it has been shown that Indians in Trinidad had an unusually high rate of diabetes mellitus. The prevalence in Indians over the age of 30 years was 6%, Wood found an even higher rate for Indians in Natal (8.8%). This prevalence rate was much higher than

for the same age groups of other races in the same area and probably higher than the prevalence among Indians in the home states of this population, which was mainly derived from 19 century emigrants from Bihar, Uttar Pradesh and Bombay.

W. Lenz, following an earlier idea of Neel, suggested as an explanation for this. that the same genes favouring diabetes under plentiful nutrition have been advantageous for the forbears of these people. The same explanation may be sought for the reported higher incidence of atherosclerotic heart disease among Singapore Indians. One may question, whether this cannot better be examined by a comparison of genetically different groups within India itself or by examination of members of the same ethnic group who stayed in their original environment and who advanced to more affluent conditions.

It should also be of particular interest to see, whether lipid disorders play the same or a different role in atherosclerotic heart disease in India, Since the prevalence of coronary heart disease in some areas seems to be low in general, environmental factors here can be assumed to be rather protective against atherosclerotic disease. People, who are affected in spite of this, to a higher percentage may show special genetic factors as for example primary hyperlipidemias. This perhaps could be tested by family studies.

There are data available on atherosclerotic disease in India which have been summarized by Pinto, Thomas, Colaco and Datey 1969. Serum cholesterol and triglycerides have been found to be lower in Indian people in general, but the cholesterol levels have shown an upward trend in recent years. This may be responsible in part for the noted increased incidence of coronary heart disease in the younger age groups. As to lipids, the authors conclude that serum triglycerides and serum cholesterol are much lower in Indian patients with ischaemic heart disease than in comparable series done in western countries, they are, however, much higher in the patients as compared to normal controls. In addition, hyperglycemia has been a common factor. No family data and no studies of lipoproteins with special techniques seem to be available till now. It certainly will be difficult to gather such data, but they would be of great general interest.

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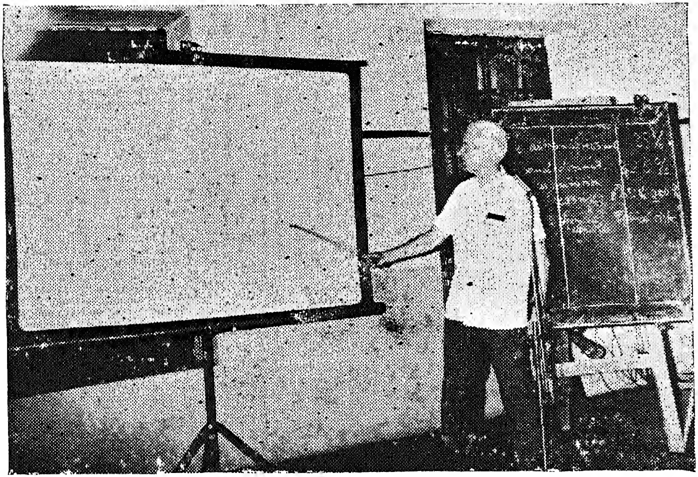

Prof. Dr. F. Vogel (Heidelberg, West Germany)
delivering the Invited Lecture

SOME ASPECTS OF BIOCHEMICAL GENETICS

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From the wide spread fields of basic research in Human Biochemical Genetics two examples should be outlined: One example dealing with a pharmacogenetic phenomenon, another one with a severe inborn error of metabolism.

Since Paulings description of sickle cell anemia as a "molecular disease" in 1949 the study of hemoglobin anomalies has given an impressive picture of genetically determined variation and has made possible the recognition of the relationship between "molecular defects" on the one hand and "clinical disorders" on the other hand.

I. PHARMACOGENETICS: PSEUDOCHOLINESTERASE POLYMORPHISMS, SENSITIVITY AGAINST SUCCINYLDICHOLINE

Interindividual different metabolisms of drugs with genetic origin are studied in a new discipline of human genetics which problems are of interest for geneticists, pharmacologists, and biochemists: Pharmacogenetics.

Genetically determined variability in response to drugs is a special form of individual difference which only becomes apparent after administration of a pharmacon. Biotransformation and detoxication of pharmaca are mostly mediated by the catalytic action of enzymes. The variation in genetic information often is the base of deferring sensitivity to drugs since the synthesis of enzymes are controlled by gene action. If the data on drug response in a randomly selected population sample are multimodally distributed into distinct classes and stability against environmental influences is known, it can be assumed that the reaction to the drug is under the genetic control of a single major gene. Interpretation of the mode of

inheritance by formal genetic models in most cases can be substantiated by studies on segregation of the trade in families.

Examples of such pharmacogenetic phenomena are for instance the reaction of individuals with certain glucose-6-phosphate dehydrogenase variants to some anti-malaria drugs or the undesirable side effect (a pheripheral neuropathy) after therapy on tuberculosis with isonicotinic acid hydrazide (INH) in persons having liver acetylases with low enzyme activity. Fig. 1 shows the multimodally distribution of plasma INH in a large number of individuals.

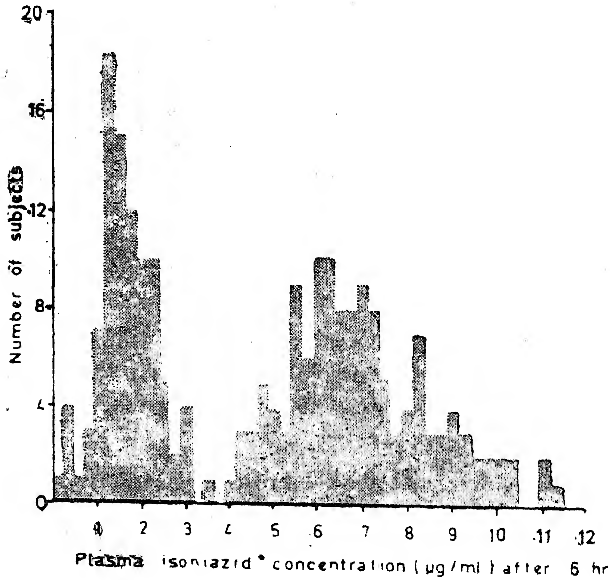


Figure 1

Interindividual different distribution of I.N.H.

One of the best known enzyme polymorphisms in regard to pharmacogenetic phenomena is the one of pseudocholinesterases. Certain variants of pseudocholinesterase provoke sensitivity to the drug suxamethonium. Individuals having such atypical variants of this enzyme show a severe and prolonged apnea after application of this drug. Chemically it is succinyl-

dicholine and this substance is of importance for anaesthesia as a short reacting relaxance.

$$CH_3 - COO - CH_2 - CH_2 - \overset{+}{N}(CH_3)_3$$

ACETYLCHOLINE

$$\begin{array}{l} CH_2 - COO - CH_2 - CH_2 - \overset{+}{N}(CH_3)_3 \\ | \\ CH_2 - COO - CH_2 - CH_2 - \overset{+}{N}(CH_3)_3 \end{array}$$

SUXAMETHONIUM

Formular of suxamethonium and acetyl-co-A

The various phenotypes of pseudocholinesterase polymorphism as well as activities, inhibition by dibucaine, clinical symptoms, and gene frequencies are shown in Table 1. A four

TABLE 1

Genotype	Phenotype	Average esterase activity, % of normal	Dibucaine number	Fluoride number	RO[2]-0683 number	Relative sensitivity to suxa-meth-onium
$E_1^uE_1^u$	U	100	71–85	57–68	>95	Lowest
$E_1^uE_1^s$	U	65	71–85	57–68	>95	Low
$E_1^uE_1^a$	I	78	50–68	42–55	58–76	Low
$E_1^aE_1^a$	A	25	14–25	18–28	<10	High
$E_1^aE_1^s$	A	20	14–25	20–25	<10	High
$E_1^uE_1^f$	UF	80	71–78	50–55	87–95	Low
$E_1^fE_1^f$	F	60	64–67	32–40	75–86	Intermed
$E_1^fE_1^s$	F	60	67	43	–	Probably Intermed
$E_1^aE_1^f$	IF	60	47-53	30–38	40–60	Intermed
$E_1^sE_1^s$	S	0	–	–	–	Highest

Pseudocholinesterase polymorphism : Genotypes ; phenotypes and their characteristics

allele model with four homozygotes and six heterozygotes can be seen. The most frequent atypical variant (phenotype A) occurs once among 2000 persons. It can be characterized by the inhibitor assay with dibucaine (affinity!). The enzyme activity measured shows a broad uni-modal distribution with the exception of atypical homozygotes and the silent gene phenotype

(fig. 2). The different frequencies for the atypical variant

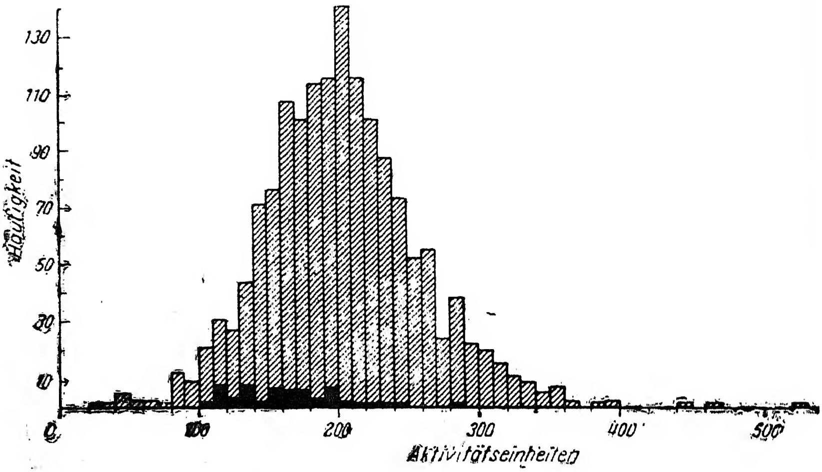


Figure 2
Unimodal distribution of activity values within different phenotypes

allele E_1^a in various populations can be seen from Table 2. The distribution of this atypical allele differs in various populations.

TABLE 2

High (> 0,014)	Intermediate (0,005-0,01)	Low (0-0,002)
North African (0,0142)	Oriental pop. mostly Japanese (0,0047)	Thais (0)
Brazilian (0,0149)	Australian (0,0051)	Japanese (0)
Greek (0,0162)	Seattle-Negro (0,0053)	Eskimo (0)
German (0,0162)	Indian (Mexican) Tribes (0,0093)	3 South Amer. Indian pop. (0)
Cauc. Americans (0,0163)	Maroccan Jewish (0,0098)	Congolese Negro (0,0009)
Portuguese (0,0168)		Formosan Chinese (0,0015)
Berber (0,0182)		Filipino (0,0024)
Canadian (0,0188)		
British (0,0192)		
Israeli (0,0312)		

Different frequencies of the atypical allele E_1^a in different populations

Considerable differences exist in regard to the affinity of succinyldicholine to the various hereditary cholinesterase enzyme variants. Fig. 3 shows the half maximum rate of

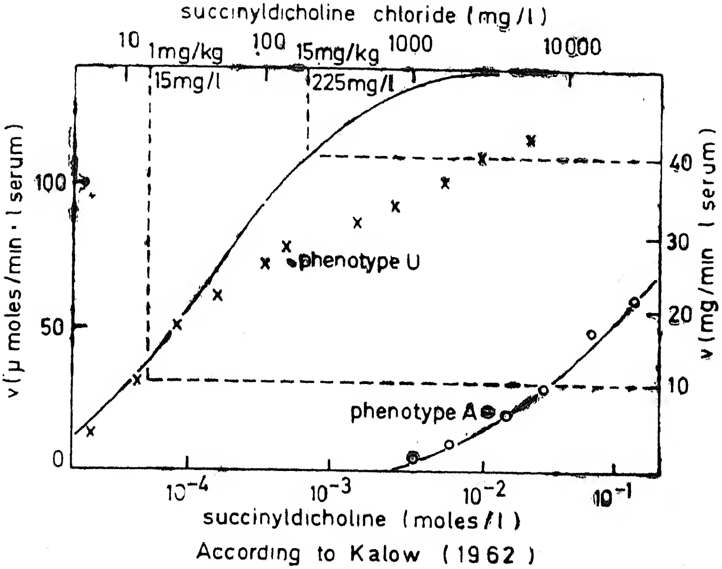


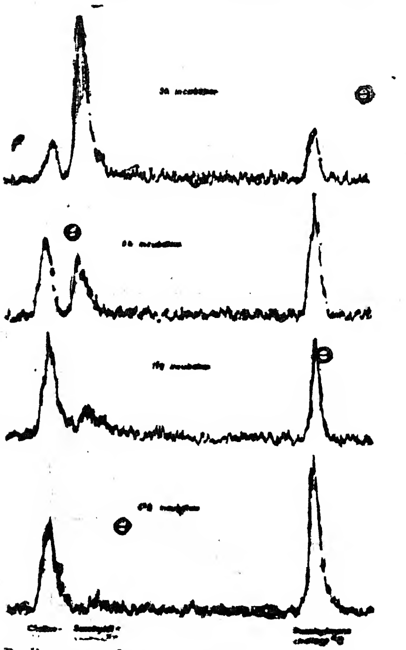
Figure 3

Difference in affinity of phenotype U and A to succinyldicholine

hydrolysis of the normal enzyme (phenotype U) and the most frequently occurring atypical variant (phenotype A) which differs by a factor of about 100; that means that the atypical enzyme cannot degrade succinyldicholine at all in those very low concentrations existing after anaesthesia. This means a prolonged apnea in persons being homozygotes for the allele E_1^a (phenotype A). This prolonged apnea in individuals having an atypical enzyme variant often lead to severe accidents in anaesthesia. Therefore it is emphasized to estimate the phenotype of individuals which have to be treated with the muscle relaxance *before* application of the drug.

We worked out a sensitive method for measuring the hydrolysis of the drug succinyldicholine at low concentrations down

to 10^{-6} M using ^{14}C–methyl–labelled radioactive succinyldicholine as a substrate which can be easily separated from its split products succinylmonocholine and choline by high voltage electrophoresis (fig. 4). Thus the kinetics of this reaction can be studied at pharmacologically interesting concentrations. Kinetic data have been studied, as for instance pH dependence of spontaneous and enzymic hydrolysis of succinyldicholine, etc. to characterise the enzyme variants (fig. 5 & Table 3).



Radiopaper electropherogram of succinyldicholine^{14}C and split products after different incubation times with serum of phenotype U (10)

Ordinate: counts per minute

Figure 4

We assume for different reasons that the enzyme pseudocholinesterase and no other serum enzyme is responsible for

TABLE 3

Substrate / Phenotype	Succinyldicholine U	A	Ratio A/U	Succinylmonocholine U	A	Ratio A/U
pH-optimum	8–9	—	—	5–6	5–6	—
K_M	$4{,}2\times10^{-5}$ (pH 7,4)	—	—	$8{,}3\times10^{-3}$ (pH 5,7)	$1{,}7\times10^{-1}$ (pH 5,7)	21
K_I Substrate: benzoylcholine (pH 7,4)	$2{,}2\times10^{-5}$	$3{,}1\times10^{-3}$	141	$4{,}4\times10^{-3}$	—	—
pI_{50}	4,1(4,01*) 5×10^{-5}M	2,1(2,02*) benzoylcholine	$\frac{I_{50}(A)}{I_{50}(U)}=99$	1,88 2×10^{-5}M	1,0 benzoylcholine	$\frac{I_{50}(A)}{I_{50}(U)}=7{,}6$

* data from Kalow

Comparison of kinetic data of the enzymic hydrolysis of succinyldicholine and succiny monocholine.

the breakdown of succinyldicholine to monocholine and choline. Only very little or no activity of succinyldicholine and succinylmonocholine can be demonstrated in sera with genetically determined cholinesterase deficiency. Regarding the affinity of

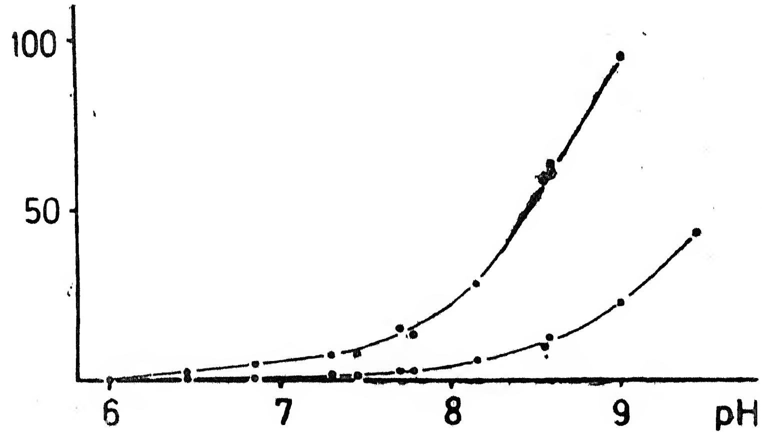


Figure 5

Dependence of spontaneous hydrolysis on pH of succinyldicholine-^{14}C (10^{-5} M, upper curve) and succinylmonocholine-^{14}C (5×10^{-5} M) at 37°. Succinyldicholine-^{14}C was incubated for one hr; succinylmonocholine-^{14}C for three hours. Ordinate: percentage relation of choline-^{14}C to substrate. Solid circles, 0.1 M phosphate buffer; open circles, 0.1 M Tris-HCl buffer; solid squares, 0.1 M glycine buffer

succinyldicholine and monocholine there are striking differences to genetically determined structural variants of cholinesterase as can be seen for succinyldicholine from Table 2: the half maximum rate of hydrolysis by the usual enzyme phenotype U and its most common atypical variant (phenotype A) differ by a factor of about 100. The enzyme activity can be precipitated by mono-specific antisera against usual pseudocholinesterase. A 10,000-fold purified cholinesterase from normal serum shows high catalytic activity to the substrate succinyldicholine.

A comparison of cholinesterase activities of 6 different phenotypes with suxamethonium on the one hand and another specific substrate, benzoylcholine on the other hand (which can

be easily measured spectrometrically) is shown in fig. 6: The values are distributed along different straight lines demonstrating the different affinities of the enzyme variants to succinyldicholine *and* benzoylcholine. A comparison of the conversion of both substrates shows a good correlation between benzoylcholine and succinyldicholine breakdown within one phenotype. Enzyme deficient sera (for instance phenotype S) show no activity with both of the substrates. So suxamethonium sensitivity

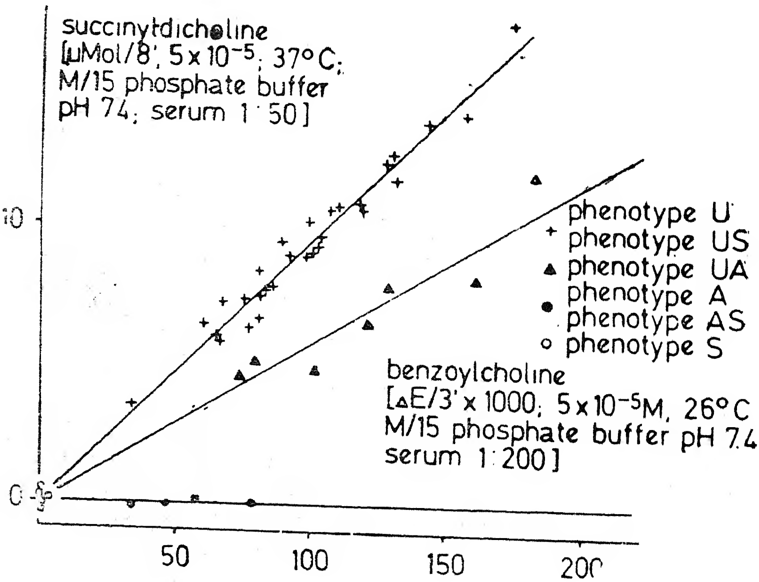


Figure 6

Comparison of activity values for different phenotypes in two assay systems: One with radioactively labelled succinyldicholin, the other one spectrophotometric measurement of benzoylcholin as substrat

of certain individuals can be measured spectrophotometrically with the substrate benzylcholine in a screening test.

The enzyme deficient, so called silent gene phenotype, shows heterogeneity, this is demonstrated in figs. 7 and 8: Here you see different pattern in disc electrophoresis within sera of 15 individuals of this phenotype and also differences in immuno diffusion tests according to Manchini.

We are starting now on the clinical symptoms and the therapy of this pharmacogenetic phenomenon. In the investi-

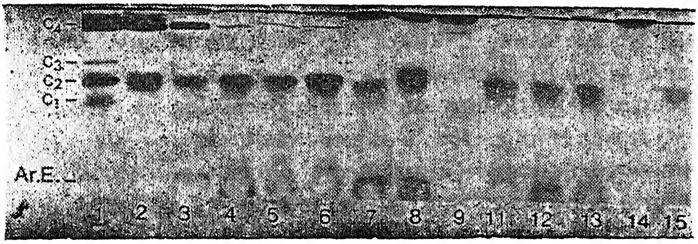


Figure 7
Discelectrophoretic differences in protein pattern within 15 sera, phenotype E_1^S

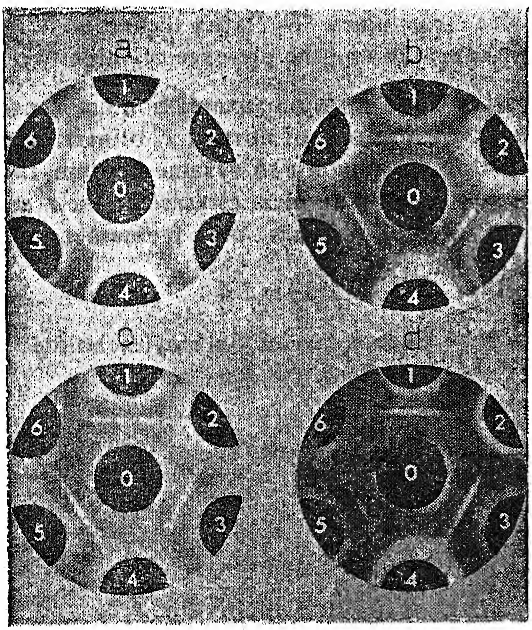


Figure 8
Different antigenic behaviour within the silent gene phenotype

gation of 182 patients showing a prolonged apnea after treatment with succinyldicholine in anaesthesia 2/3 showed atypical

cholinesterase variants which pointed to a hereditary enzyme defect (Table 4). Here are reports from Kalow and from Whittaker. Comparatively high differences are found regarding the observed and expected frequencies: Approximately 1/3 of the cases with a prolonged apnea do not show any hereditary variants of cholinesterase. This has been discussed during the II. International Workshop on Pharmacogenetics in Titisee/Germany. It was emphasized, using the methods for detection of the known genetically determined cholinesterase variants other structural mutants of this enzyme may be overlooked on the way that the enzyme appears to be normal, but does not react with suxamethonium at pharmacological concentrations. Probably the best way to identify genetically determined cholinesterase variants causing suxamethonium sensitivity, would be to measure the enzymic hydrolysis of this drug directly, comparing the results with those of standard assays or of quantitative immunological techniques. The latter technique is independent from kinetic variation and the presence of inhibitors in serum.

From all data we know on suxamethonium sensitivity one would expect that injection of normal cholinesterase activities should normalize the response to suxamethonium in those 2/3 of patients who have an atypical esterase in their serum. The infusion of fresh plasma has been recommended by some

TABLE 4

Pche Phenotypes of Succinyldicholine Sensitive Persons

Phenotypes	Genotypes	n (Kalow)	n (Whittaker)	Total	Observed	Expected
U	$E_1^uE_1^u$	39	25	64	35%	~95.5%
UF	$E_1^uE_1^f$	1	6	7	4%	<0.5%
UA	$E_1^uE_1^a$	11	10	21	11.5%	4%
AF	$E_1^aE_1^f$	2	7	9	5%	0.005%
A	$E_1^aE_1^a$	50	30	80	44%	0.03%
AS	$E_1^aE_1^s$	—	—	—	—	—
S	$E_1^sE_1^s$	1	0	1	0.5%	0.001%
		104	78	182	100%	~100%

authors, however a convincing positive effect has not been described. Borders in 1955 reported the shortening of the duration of apnea by injecting cholase (concentrated serum cholinesterase) *before* the application of suxamethonium. However, injection of cholase during relaxation shows no abbreviation of apnea.

Our own experiments show that therapy of the prolonged apnea in persons with atypical cholinesterase is possible by injection of purified normal cholinesterase before *and* shortly after application of suxamethonium.

TABLE 5

Therapy of Prolonged Apnea with Purified Pseudocholinesterase (Pche)

Case	Before injection of Pseudocholinesterase			After injection of Pseudocholinesterase*		
	Time of apnea (mg suxamethonium/kg)	PCHE-activity (benzoylcholine)	PCHE-phenotype	Time of apnea 1st muscle contraction	Respiratory volume >350ml	PCHE-activity (benzoylcholine)
1	45′ (0.5)	38	A	5′	6′	128
2	75′ (1.0)	49	A	8′	10′	114
3	110′ (1.0)	28	AS	10′	11′	96
4	210′ (1.0)	50	A	9′	12′	133
5	150′ (1.0)	55	A	7′	12′	113
6	98′ (1.0)	36	A	9′ **	11′ **	122
Mean	115′	43		8′	10′	118

* PCHE was injected 16′ after application of 1 mg suxamethonium/kg
** PCHE was injected before application of 1 mg suxamethonium/kg

It is a practical example for the fact, that a genetically determined enzyme defect can be overcome by normalizing the metabolic disorder through application of the lacking normal enzyme. Besides treatments in gastroenterology, which, however, are unspecific, this is the only known example of a logical therapy of an enzyme defect by substitution with a highly purified active enzyme. Some of our results can be seen from Table 5. Three of the six cases mentioned here became known by

showing a prolonged apnea after anaesthesia during an operation. The others were detected as having the atypical enzyme in a screening test of sera from about 10.000 blood donors.

The narcosis were started with a short acting barbiturate, N_2O and 1 milligram per kilogram bodyweight of suxamethonium. 16 minutes later – that is about twice the time of normal relaxation after this dosage of the drug – the whole plasma activity of cholinesterase, calculated from individual plasma volume, and normal enzyme level has been injected. 1300–fold purified enzyme preparations from human plasma were used. These preparations from the Behring Company are free of Australia antigen, polyoma – and Newcastle disease viruses, and no pronounced imcompatibility reactions have been observed.

In the three persons who were found by the routine investigations and who were, never been treated with suxamethonium before, control narcosis were made about two months later, to estimate their individual duration of apnea: the same amount of suxamethonium was injected but this time without application of normal purified cholinesterase. Now the apnea lasted about two hours.

The interruption of prolonged apnea by injecting purified cholinesterase prior to narcosis could not be possible if there would exist an inhibitor for the enzymic succinyldicholine hydrolysis in serum as postulated by Pilz. However, Pilz was not able to show an enzymic conversion of suxamethonium in human serum and postulated the breakdown of the drug to be catalysed by an enzyme of the lung. Results of experimental narcosis do not exclude that *besides* the serum cholinesterase there may exist another enzyme, for instance in the lung, which could be responsible for the breakdown of suxamethonium. If there, however, could be a suxamethonium splitting enzyme in the lung this also should be deficient in patients having genetically determined enzyme variants in serum. This means that the genetic information controlling the structural variations of the serum enzyme also controls the corresponding enzyme in lung or some other organs. In fact it has been demonstrated by Dr. Lehmann's and Dr. Kalow's group that the cholinesterase activity in different organs is controlled by the same locus which is responsible for synthesis of the serum

enzyme. Furthermore it has been rather clearly demonstrated by Doenicke et al in a case of genetically determined total enzyme deficiency that the liver cholinesterase was also totally deficient.

We recently tried to use purified cholinesterase to get some more knowledge concerning the nature of organo-phosphate poisoning. The esterase was injected to a patient three weeks after intake of the insecticide parathione (E 605) for a suicide. At this ime the patient still got artificial respiration and the serum activity of cholinesterase was zero. On figure 9 it is demonstrated that the enzyme level in the serum after the first injection rose to 40% and afetr a second injection to 70% of

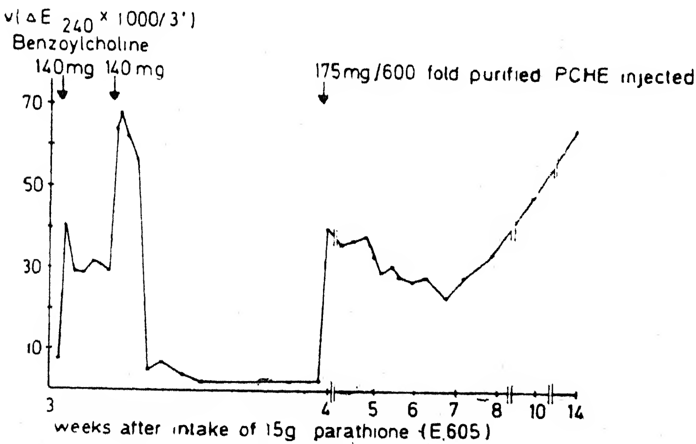


Figure 9

Serum cholinesterase activity of a patient poisoned with 15 g parathion. Ordinate: enzyme activity (substrate: benzoylcholine 5×10^{-5} M; units: $\Delta E_{240} \times 1{,}000/3'$; 26° C, M/15 phosphate buffer pH 7. 4; serum dilution 1 : 200). Abscissa: weeks after intake of the organophosphate. Arrows indicate application of purified human cholinesterase

normal values until at the fourth day the activity dropped to zero again within six hours. An immunological rejection was excluded by various arguments. A few days later purified esterase was injected again. From this time on nothing similar happened and the patient got over the bad condition accompanied by the rise of his own cholinesterase activity. The

symptomatics of organo-phosphate poisoning are quite different from patient to patient. Often one cannot explain the bad condition of the patient weeks after intake of the insecticide on the assumption that the compound will be excreted within a few days. The observations demonstrated in figure 9 as far as we know best fits well with the assumption of irreversible inhibition of cholinesterase by an inhibitor usually not found in tody fluids : for instance by residual organo-phosphates like the insecticide parathione.

Some other pharmacogenetic phenomena may be mentioned on the end in the following Table 6. It includes only some

TABLE 6

Examples of Pharmacogenetical Phenomenons

Deficiency of Glucose-6-phosphate - Dehydrogenase (sensitivity for primaquine ; favism ; hemolytical anaemia after application of sulfonamides)
Hemoglobine – Zurich–Syndrome (position 63 of β–chain, histidine replaced by arginine ; hemolytical anaemia after application of sulfonamides)
Vitamine D – resistent rachitis (x – chromosomal heredity ; 20 – 100 – fold dose of vitamine D necessary)
Extrapyramidal disturbance after application of phenothiazines; after FISHER and GRIFFIN there is a direct correlation to the sensitivity for certain bittertasting substances, e. g. chinine and amphetamine, correlation between taste thresholds in human beings and poisons in animals
Different effect of antidepressive substances (inhibitors of monoaminooxydase, imipramine)
Porphyria intermittence acuta after application of narcotics (e. g. barbiturates) and sulfonamides (autosomal dominant heredity); disturbance in metabolism of σ–aminolevulic acid
Genetically determined polymorphism of bitter-tasting (phenylthiocarbamide and anetholtrithione)

Correlation between red-green-acromatopsia, alcoholism and cirrhosis hepatis
Polymorphism of various anaphylactical reactions after injection of dextrane in rat

of so many interesting pharmacogenetics phenomena; for instance also the coumarine resistance in man, the acetylation polymorphism due to isonicotinic acid hydrazide, serotonin and some other substances, the acetophenetidin incompatibility, the increase of intraoculor pressure after local application of dexamethasone and the interspecies variability of drug metabolism in regard to atropin, phenylbutazon, antipyrin, aethanol etc. have been studied in the last years.

With reference to the "bitter taste" we have discovered a new substance, anethol trithione which has a completely different constitution in comparison to the well-known thiocarbamides and which shows exactly an analogue genetically determined polymorphism.

According to the large amount of drugs yearly put on the market it is expected that there will occur a great number of unwanted side effects. The detoxication of these unphysiological substances is not always possible via normal metabolic pathways of the organism. Besides these pharmaca often led to an unwanted inhibition or induction of biologically important ways of metabolism. In that way a special therapy will be put in question many times, as well as by the above mentioned pharmaco genetic phenomena.

II. Inborn Errors of Metabolism : Maple Syrup Urine Disease

This is a metabolic disorder for the degradation of branched chain amino acids. Such genetic defects of amino acid metabolism are studied to a minor extent, mainly because of the difficulties in obtaining sufficient material for enzyme studies. However, a rather large and almost increasing number of new detected inborn errors have been described in the last years (fig. 10).

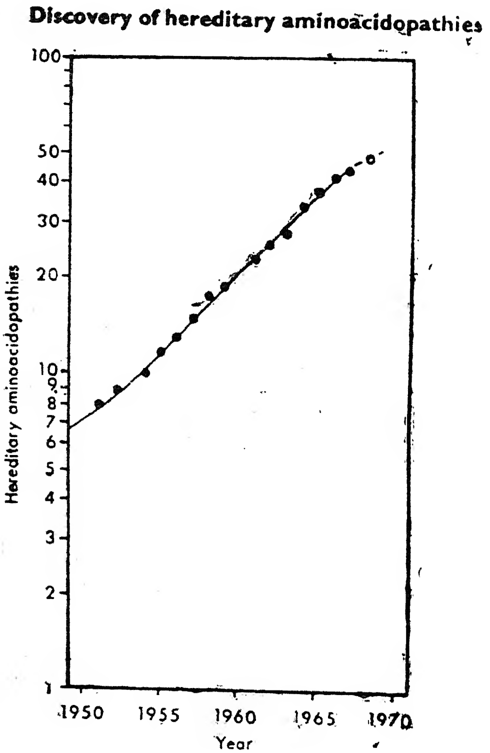


Figure 10
Ordinates : cumulative number of hereditary aminoacidopathies
Exponential rate of discovery reflects adaptation of chromatographic methods to clinical investigation in man (Dent, 1946)

Some of them and their frequencies are shown in the next figure (Table 7). Calculations of frequencies of diseases like

TABLE 7

The Most Common Inborn Errors of Metabolism in Caucasian Populations (According to W.H.O. 1968)

Cystic pancreas fibrosis	1 : 1500 - 8000
Hyperphenylalaninemia (2/3 classical P.K.U.)	1 : 10 000
Galactosemia	<1 : 25 000
Adrenogenital Syndrome	1 : 67 000
Hepatolenticular Degeneration (Wilson)	<1 : 100 000
Maple Syrup Urine Disease	1 : 300 000

these are very difficult and, therefore, we have to assume that the frequency often is much higher than we know at that time. Furthermore some diseases which have been known for a longer time have been differentiated in certain types by better techniques in biochemical and clinical diagnosis, for instance galactosemia, phenylketonuria, and maple syrup urine syndrome.

Heterogeneity might be rarely common in genetically determined enzyme defects. This has been shown especially in glucose–6-phosphate–dehydrogenase deficiency by detection of nearly a hundred different protein variants.

In the case of maple syrup urine disease the oxidative decarboxylation of the three branched chain keto acids (fig. 11)

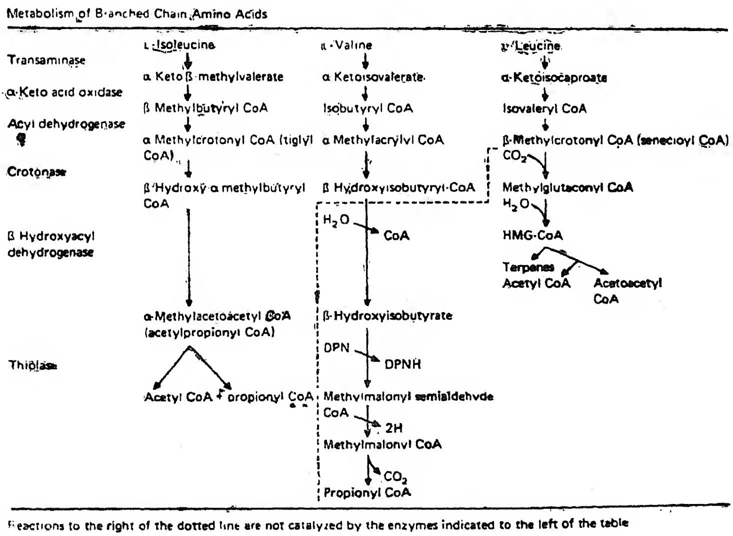


Figure 11

Metabolism of the branched chain aminoacids and oxoacids

such as ∝-ketoisocaproic acid, ∝keto-β-methylvaleric acid, and ∝keto-isovaleric acid are blocked. This is demonstrated in a simple way from the next figure (fig. 12). The concentrations of these keto acids and their corresponding amino acids, leucine, valine, and isoleucine are elevated and cause brain damage and retardation. These keto acids and amino-acids can be

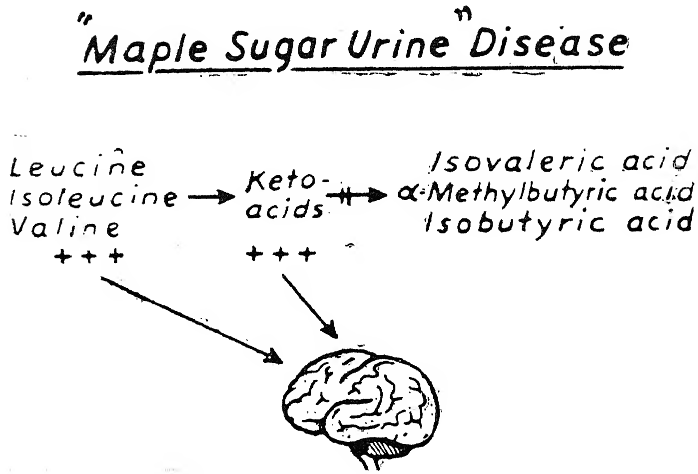


Figure 12
The metabolic block in maple sugar urine disease

estimated for diagnosis in the plasma and the urine from such patients in a way, which is shown in (fig. 13).

The patients must have a special diet with very low concentrations of leucine, isoleucine and valine, otherwise they die. The next Table (Table 8) shows a combination of food which often is used as a diet for patients with maple syrup urine disease.

TABLE 8

Specimen Diet for a 7-Month Old Patient with Maple Syrup Disease

Maple syrup disease	7 months, 7.0 kg. BW
200 g. Whey 20 g. L-Aminoacids 30 g. Cornflour 40 g. Sugar 60 g. Butter 150 g. Carrots 5 g. Yeast 600 g. Tea	Leucine 30 mg./kg. BW Isoleucine 22 mg./kg. BW Valine 22 mg./kg. BW
Vitamins & Minerals	

The defect can be recognized very early (and this is of great importance!) analogue to some other genetically

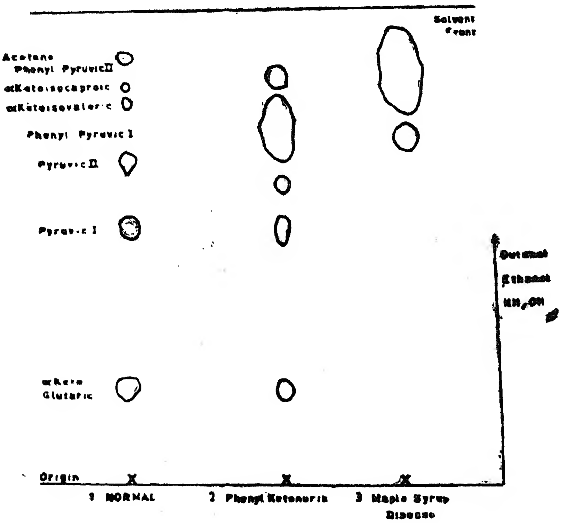


Figure 13

Replica of the Urinary Keto Acid Chromatogram in 1. Normal infant, 2. Infant with phenyl ketonuria and 3. Infant with maple syrup disease.

The keto acids are precipated inform of their 2, 4 dinitrophenyl-hydrazones, which are subjected to chromatography, Whatman 40 paper, descending chromatography. Butanol 130 parts, ethanol 20 parts, 1 M NH_4OH 50 parts. Spots identified by their intrinsic color, and outlined under ultraviolet light.

determined diseases as for instance are shown in the next Table (Table 9).

TABLE 9

Inborn Errors of Metabolism Manifesting with in the First Week of Life

Maple Syrup Urine Disease
Hyperglycinemia
Isovaleric Acid Disease
Arginine Succinic Acid Disease

Up to now four types of maple syrup urine syndrome are differentiated as to be seen in the next Table (Table 10). These

TABLE 10

Different Forms of Maple Syrup Disease

1) Classical type with elevation of concentration of Leucin and α-keto-isocapronic acid (Menkes et al. 1954)
2) Classical type with increase of α-keto-β-methyl-valeric acid (Antener 1969)
3) Intermittent type with reduced enzyme activity (Morris 1966, Dancis and Rokkones 1967, Goedde et al. 1970)
4) Reduced enzyme activity without intermittent course (Seegmiller 1970)

different types within the socalled maple syrup urine disease are another example for heterogeneity within genetically determined diseases. Some years ago we could show that the enzymic activities of branched chain keto acid oxidases can be measured directly by incubation of vital leucocytes with branched chain keto acids which are ^{14}C–radioactively labelled on the carboxyl-group. The $^{14}CO_2$ which is liberated from the carboxyl-group can be measured. The enzyme activity of children which are atypical homozygotes in regard to the classical form of this disease is about zero. Their parents are heterozygotes and show a reduced enzyme activity of about 50% with all three keto acids as substrates (Table 11). Therefore the

TABLE 11

Conversion of Branched Chain Oxoacids with Enzymes from Leucocytes of Normal Homozygous and Heterozygous Persons

Oxoacid	Converted substrate (mμ Mole/ 1.6 × 10^7 leucocytes) normal homozygotes			heterozygotes		
	n	mean	standard-deviation	n	mean	standard-deviation
α-oxo-isocaproic acid	71	3.25	0.72	39	1.47	0.46
α-oxo-isovaleric acid	32	4.04	0.78	29	1.79	0.61
α-oxo-β-methylvaleric acid	27	3.09	0.78	27	1.44	0.34

classical type of maple syrup urine syndrome shows an autosomal recessive trait (fig. 14).

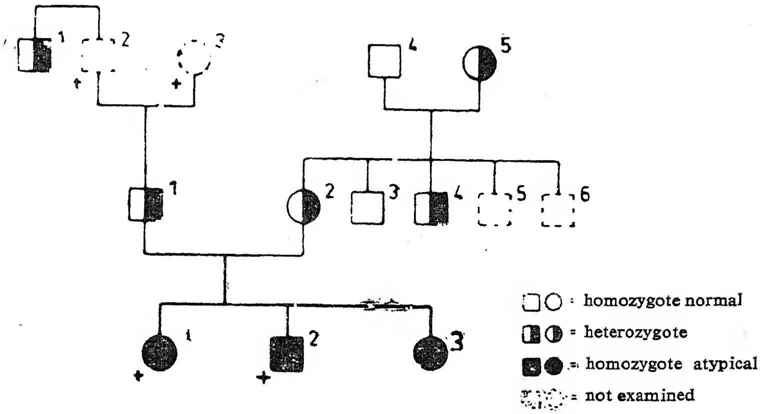


Figure 14

Pedigree from a family with classical type of Maple Syrup Urine Syndrome

Three cases from another type of this disease could be investigated in the last years by our group: The socalled intermittent type of maple syrup urine disease. The explanation of genetics in these cases is much more difficult. In children who are atypical homozygotes a residual enzyme activity is observed. On the other hand only one of the parents in the intermittent type shows a decrease of enzyme activity to about 50%. The other one shows a rather normal activity value. The next two figures (15,16) show pedigrees of such families.

We suppose that patients of this type of the disease may have *two different* alleles, one of which may not be detectable for recognition of heterozygotes with our methods. Analogue findings are known from the literature in regard to enzyme variants of pyruvatekinase deficiency and galactosemia. In these cases an interallelic complementation may be discussed.

The genetic analysis of maple syrup urine syndrome is now much more easier after our finding that the keto acid oxidases

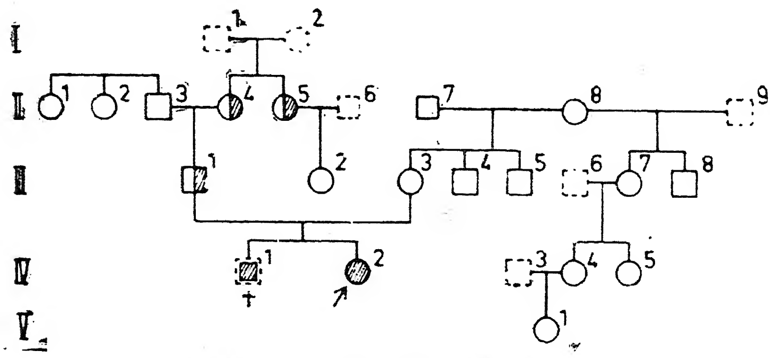


Figure 15

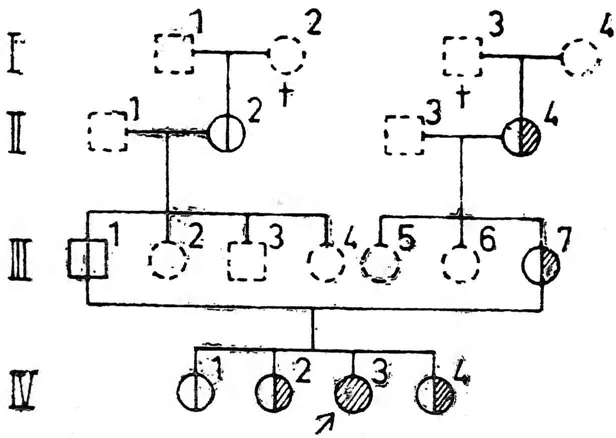


Figure 16

Pedigree of family with the intermittent type of Maple Syrup Urine Disease

Symbols used in Figs. 15 and 16 : ⬚, not studied ; □ studied, normal enzyme activity ; ◐, studied, enzyme activity about 50% of normal ; ▨ patients.

in peripheral blood are localized mainly in the lymphocytes. Using heterozygote assays with leucocytes one generally has to put into consideration the possibility of different localisation

of the enzyme proteins. For example O'Brien pointed out that the enzyme sphingolipid degradation are essentially localized in neutrophiles.

We recently used the assay technique mentioned above with fibroblast cell lines from the skin of patients with maple syrup urine disease in comparison with cell lines from normal persons. It has been shown clearly that the diagnosis of this disease may also be performed in cultured cells: atypical homozygotes show no enzyme activity for branched chain keto acid oxidases.

A satisfactory diagnosis of heterozygotes, however, is often not possible in fibroblast cultures with the techniques used at the present time: the values intraindividually as well as interindividually show considerable variation. This has been reported by other authors too, as for instance from the group of Dr. Gartler, Seattle and Dr. Dancis, New York, who had the same differences regarding the considerable variability of their values.

In the fibroblast cultures of patients with maple syrup urine disease (classical and intermittent type) the activity of pyruvic oxidases is in a normal range whereas in homozygotes of the classical type there is no activity of branched chain keto acid oxidase at all and only a residual activity in homozygotes with the intermittent type. This means that in these patients the oxidative process in pyruvic acid metabolism and the citrate acid cycle is not disturbed. We know some biochemical background of these severe inborn error of metabolism, too. According to experiments with multienzyme complexes from streptococcus faecalis as a model the branched chain keto acid oxidases seemed to have an analogue confirmation as the well-known pyruvate oxidase complex. The next figure (fig. 17) shows an electron optical interpretation of the protein of the pyruvic oxidase enzyme complex, which first has been given by Reed. There are three different protein units of the multienzyme complex which is responsible for oxidative decarboxylation

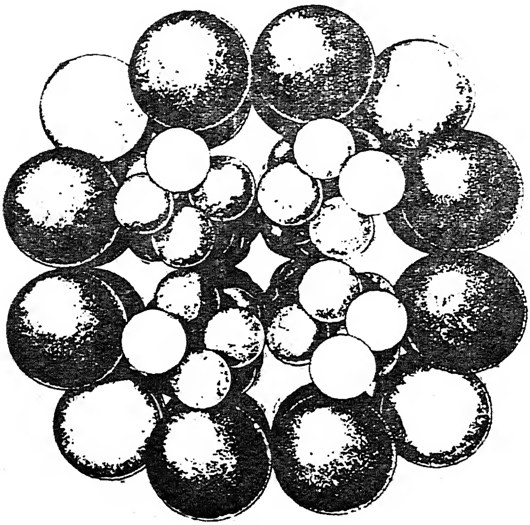


Figure 17

Model of the structure of pyruvate dehydrogenase. Large spheres: pyruvate dehydrogenase; Medium spheres: lipoamide oxidoreductase; Small spheres: subunits of the lipoic acid reductase-transacetylase (Reprinted from *Science 145*:930 (1964) with permission of the copyright owner).

of the keto acids (Fig. 18). The measurement of those enzyme units is possible independently from each other. One enzyme unit of the multienzyme complex of keto acid oxidases, the thiamine pyrophosphate containing decarboxylase, can be assayed using unphysiological electron acceptors such as dichlorphenolindophenol and ferricyanide. Another protein unit of the complex, the flavine enzyme lipoamid oxidoreductase (or lipoic acid dehydrogenase)reoxidases the protein-bound co-factor lipoic acid in the presence of N.A.D. ; this can be measured spectrophotometrically. The transacylase, the third enzyme unit contains lipoic acid and catalyses the transfer of the acyl group from the "active aldehyde" which contains thiamine

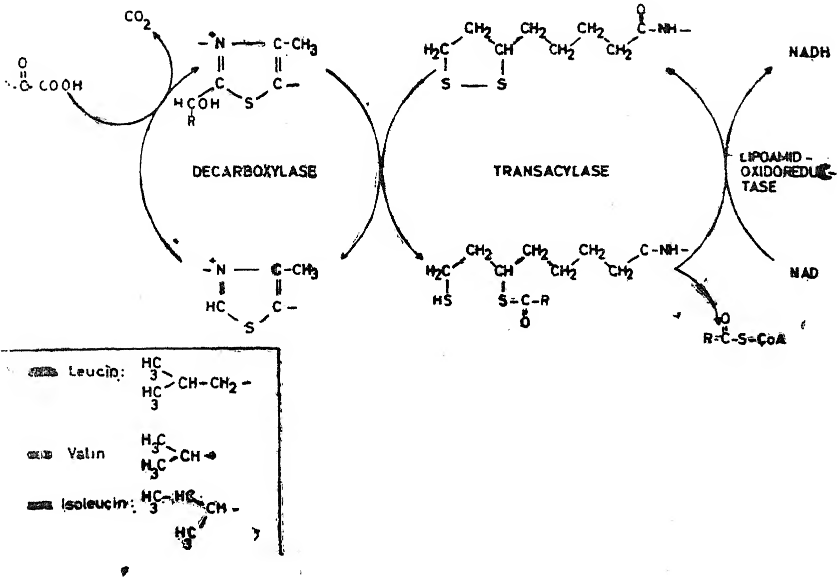


Figure 18
Reaction sequence of oxidative decarboxylation : participation of the three protein units of the multi-enzyme complex, decarboxilase, transacelase, lipoamidoxidoreductase

pyrophosphate to coenzyme A (Fig. 19). The so called

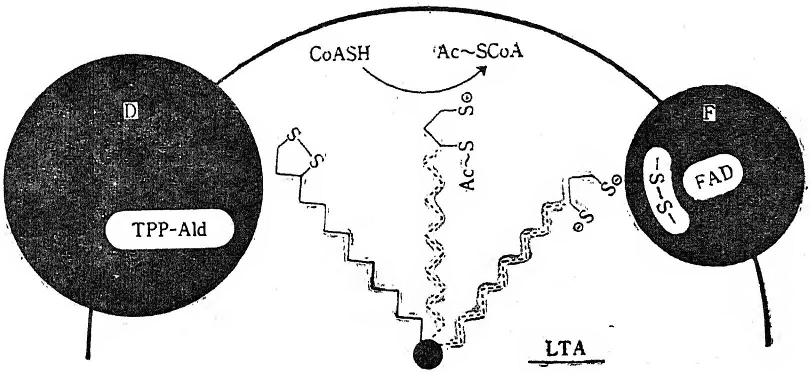


Figure 19
A schematic representation of the possible rotation of a lipoyllysyl moiety between α-hydroxyethylthiamine pyrophosphate (TPP-Ald) bound to pyruvate dehydrogenase (D), the site for acetyl transfer to CoASH, and the reactive disulfide of the flavoprotein (F). The lipoyllysyl moiety is an integral part

hydroxamate assay can be used here (see fig. 20).

Certain experiments permit to release lipoic acid specifically from the transacylase protein by lipoamidase. A recombination of the complex with radioactive labelled ^{35}S lipoic acid is possible by catalysation with a lipoic acid activating system. After splitting of lipoic acid, the activity of the decarboxylase is unchanged, however, the total reaction is disturbed.

The next figure (fig. 20) shows the overall reaction for measuring the oxydative decarboxylation of keto acids and a

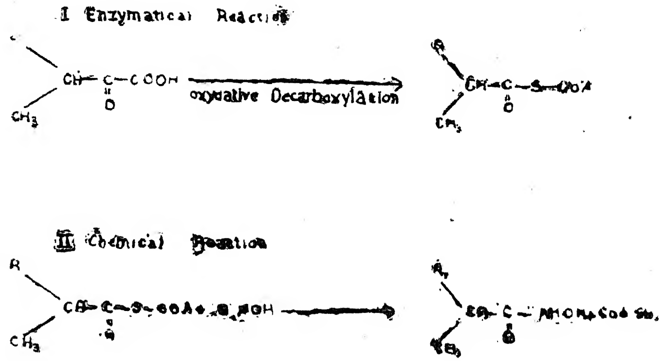


Figure 20

I. Overall reaction of oxidative decarboxylation; II. Formation of hydroxamate from acyl-co-enzyme A

partial reaction using the socalled hydroxamate reaction mentioned above. The acyl-co A-ester which is built in the main reaction, shown in the upper part of the figure, can be transferred then to a hydroxamate. The latter substance can be differentiated and separated by thin-layer-chromatography techniques and then can be estimated quantitatively in a radioactivity scanner. This is another possibility for diagnosis of the disease and for measuring different reactions of the multienzyme complex to get some more knowledge of the detailed mechanism of this enzyme defect of branched chain amino acid metabolism.

The Purification of such keto acid oxidases from human kidneys has shown that the enzymes from human organs catalyzes the same test reactions as that from bacteria. The

decarboxylase assay with dichlorphenol-indophenol, the lipoic acid dehydrogenase reaction, the acyl transacylase reaction, and the total reaction of keto acid oxidase multi-enzymes have been measured, too. The question that there are different multi-enzyme complexes for branched chain keto acid degradation on the one hand and pyruvate degradation on the other hand seemed to be clear. However, it cannot yet be decided exactly if there are three different branched chain keto acid oxidases for the pathways of leucin, isoleucin or valine or not.

In general, what has to be done after detecting a new genetically determined disease? One needs a special assay for the diagnosis of atypical homozygotes *and* heterozygotes. This assay must be possible to perform in body fluids and not in organ material; the latter mostly is very difficult or impossible to get. This assay has to be done very quickly and soon after birth. Then a therapy must be developed – often a diet – which has to be applicated mostly in the first days or weeks of life. The kind of genetic trait which has to be investigated (it may be recessive, dominant, X-chromosomal etc.) to have the possibility for genetic counselling to the parents after heterozygote diagnosis.

Basic research, mostly with biochemical methods, has to be performed which often is the supposition for a therapy. For instance the detection of an enzymatic block shows, what diet has to be given to avoid high concentrations of intermittent metabolites which cannot be degraded because of the lacking enzyme and which often causes cerebral poisoning and retardation. Mostly these different steps often have to be done in team work: by clinicians, geneticists and biochemists.

POLYMORPHISM OF β-LIPOPROTEINS INVESTIGATIONS OF THE Lp(a)-VARIANT

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(Institute of Human genetics - University of Marburg - Marburg/Lahn, West Germany)

Genetic markers in human plasma became of considerable interest in the past not only for several questions of human genetics but also were used as valuable tools in the field of biochemistry.

The importance of genetic variants for the understanding of the molecular biology of proteins has been demonstrated especially by the investigations of immunoglobulins.

Similar as in this class of serum proteins - at least from a formal genetic point of view - two completely independent serum group systems have been described within β-lipoproteins of human serum, the Ag - and the Lp-system. Both of these originally were demonstrated by means of specific immune-antisera.

THE Ag-SYSTEM

In the case of the Ag-system these antisera are isoimmune-sera, that means antisera, that have been raised in men by multiple transfusions. Antibodies against Ag-factors especially are found in polytransfused patients suffering with thalassemia and other haemolytic diseases.

There have been many attempts to produce anti Ag-antibodies in animals, but all failed. The Ag-polymorphism first described by Allison and Blumberg (1961) originally was demonstrated by a precipitation reaction in agar gel the double-diffusion test of Ouchterlony (1958). Sera-exhibiting a precipitation line with the anti-Ag-antiserum were called Ag(a+), those giving no reaction Ag(a$^-$).

The authors gave evidence for an autosomal dominant inheritance of the Ag-factor.

Subsequently Hirschfeld (1963) was able to show by proper absorption experiments that the original-antiserum (C de B) of Allison and Blumberg contained at least three different antibodies thus reacting with three different Ag-factors. Bütler and Brunner (1966) by introducing the haemagglutination inhibition test for Ag-typing not only presented a refined investigation technique in this field of research but also were able to demonstrate non-precipitating anti-Ag-antibodies. At present nine different factors are known in the Ag-system.

All these antigens are inherited as autosomal dominant traits. Evidence for the existence of pairs of allels at four closely linked loci namely the Ag a_1/d, the Ag c/g, the Ag x/y and the Ag t/z loci was given by Morganti, Beolchini, Bütler, Brunner and Vierucci (1970) and by Hirschfeld and others (1969).

The 9th factor Ag(m) was demonstrated to be closely linked to the other ones by Contu (1968), but an antithetical factor has not been found yet. Thus Hirschfeld pointed out that the Ag-system might constitute a complex genetic system analogues to the model proposed by Race and Fisher for the Rh-system.

Even if the genetics of the Ag-system are well established there are some unresolved questions. As pointed out by Hirschfeld less than 28 of the 81 expected phenotypes assuming a model of two allels at four closely linked loci - have been observed despite examination of large samples.

Nothing till now is known on the chemical nature of the Ag-determinants that means on those regions of the β-lipoprotein-molecule that differ in various Ag-phenotypes.

The Lp-system

The Lp(a)-lipoproteins represents a further variant of the β-lipoproteins of human serum. It was discovered by means of absorbed heteroimmune antisera of the rabbit by K. Berg (1963), who could also show the heredity of the occurrence of this lipoprotein.

As in Ag, the Lp(a) - factor was originally demonstrated in Ouchterlony test, that allowed differentiation between two types of human sera, Lp(a+) and Lp(a-). Gene frequency for the autosomal dominant gene Lp^a was estimated by Berg in an Norwegian population to be 0.1948.

Studies on the population genetics of the Lp(a) factor were reported by Berg and by Wassenich. These demonstrated that there are marked differences between the main races. There were reported high frequencies of the Lp(a) gene in Negros, low ones in Mongol populations, whereas the frequencies of Caucasians were in between. Extremely low values were observed in the native population of the Eastern Islands and in Labrador Indians (Berg, 1968). It should be pointed out, however, that one must be extremely cautious in interpretation of these findings because lipoproteins are very instable and sensitive to temperature and freezing. That means: valid values are only obtained by examination immediately after blood has drawn. Moreover there can be only compared studies were standardized or the same anti-Lp(a) antisera have been used. The cause for this may be found in the following observations.

There have been found frequencies of Lp(a+) phenotypes within German populations differing from 29% found by Jörgensen in Göttingen, 47% found by Renninger and co-workers in Marburg, to more than 50% by Seidel in Frankfurt. This differences cannot be explained by differences in the population but only by those in the anti-sera. Furthermore there have been reported higher frequencies of Lp(a) in patients suffering from coronary heart-disease and such with diabetes mellitus and in pregnant women, whereas lower values were observed in patients with liver diseases as cirrhosis and hepatitis. In these patients there have been reported changes in Lp(a) phenotype during the course of illness (Jörgensen).

Thus there was given strong support for the idea that environmental factors might influence Lp(a)-frequencies.

Moreover when at first glance it looked as if there could be made a clear cut distinction between Lp(a+) and Lp(a-) types, Renninger and co-workers pointed out the occurrence of weak reactors and the difficulty in their interpretation.

Comparative studies of 17 different anti-Lp(a)-antisera by the same material of pannel sera in our laboratory demonstrated that the marked differences in frequencies were almost exclusively dependent on the demonstration of weak positive reactors.

From this and other observations to be discussed later it was concluded, that the Lp(a)-lipoprotein represents not a qualitative but a quantitative variant of β-lipoprotein.

Biochemistry of Human Serum Lipoproteins

Before representing our recent knowledge on the chemical composition and immunological properties of the Lp(a)-lipoprotein, it may be helpful to give a brief general introduction into the field of human serum lipoproteins.

Lipoproteins because of their high lipid content represent the protein class of lowest density in serum. Subdivision of lipoproteins commonly is achieved by means of (1) their flotation behaviour in ultracentrifugal analysis, (2) their mobilities in different kinds of electrophoresis and (3) by their immunological properties.

The historical development of the different techniques allowing classification of lipoproteins, led to a babylonic confusion of nomenclature in lipoprotein chemistry that has not yet been overcome.

That is why it must be stated that all these characteristics, together with their chemical composition will define the different types of lipoproteins. Especially increasing information on the polypeptide composition of apolipoproteins i.e., aminoacid composition and end-group analysis etc., as revealed in the last few years by several laboratories provide a classification mainly based on the chemical properties of the apolipoproteins (Fig. 1).

There are two main classes: 1. The Low-Density-Lipoproteins, abbreviated LDL with density below 1.063 g/ml; 2. The High-Density-Lipoproteins = HDL in the density range from 1.063 – 1.21 g/ml.

The low-density-lipoproteins can be subdivided by their flotation behaviour into the chylomicra, the Very-Low-

Density-Lipoproteins (< 1.006 g/ml) with pre-β-mobility in agarose gel electrophoresis, and the LDL_1 - (1.006 - 1.019 g/ml) and LDL_2 - (1.019 - 1.063 g/ml) fractions.

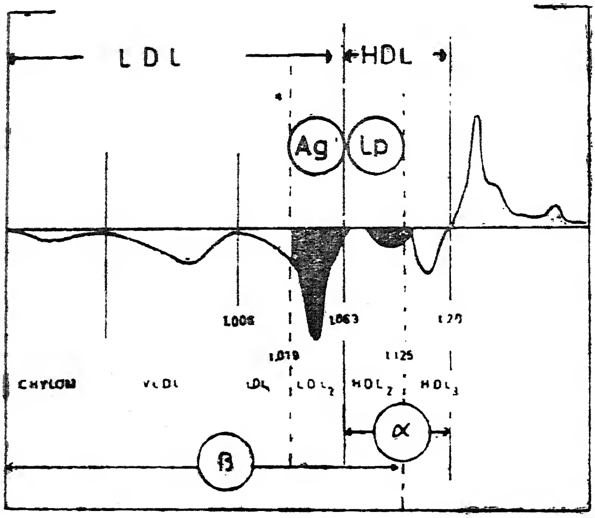

Figure 1

The division of lipoproteins into density-classes as it is achieved by analytical ultra - centrifugation studies

All these lipoproteins immunologically react with anti-β-lipoprotein antisera and despite their well-known immunological, electrophoretical and chemical heterogeneity often are referred to as β-lipoprotein.

The low-density-lipoprotein within a density range of 1.019 - 1.063 g/ml represent the main component of β-lipoprotein in normal persons. It is composed of about 78% lipid, 20% protein and some carbohydrate. Molecular weight was estimated independently by Margolis and Langdon, Scanu and co-workers and Adams and Shumaker to be about 2.3×10^6.

One of the main limitations upto now on investigating low-density-lipoprotein structure is the difficulty to obtain a water soluble protein moiety (=apoprotein), without using detergents as Sodium-dodecylsulfat that cannot be completely

removed after delipidation, without chemical modification, or thirdly without getting a highly aggregating material. Thus molecular weights of the protein subunits were estimated from about 36.000 to 80.000 (Scanu, Day and Levy); As N-terminal aminoacids there have been described mainly glutamic acids, serin and alanin by several authors (Fredrickson and co-workers, Scanu and co-workers, Shore and Shore).

There have been employed a variety of different techniques to isolate LDL_2, as for example preparative ultracentrifugation, precipitation by polyanions, column chromatography on hydroxyl - apatite as well as sepharose gel filtration. Commonly there are used combinations of these techniques.

The HDL-class is subdivided into density classes HDL_2 (1.063 - 1.125 g/ml) and HDL_3 (1.125. - 1.21 g/ml). Both mainly consists of a material moving in α_1-position in agar gel electrophoresis.

There have been demonstrated minor lipoprotein components under normal as well as pathological conditions that will not be mentioned here.

On the basis of their chemical composition and immunological properties three main types of apoproteins can be distinguished, each of which has been shown to be heterogenous in respect to its polypeptide composition (Gustavson et al., Scanu and co-workers, Fredrickson et al). These are the apolipoproteins A, B and C. Recent data from Seidel and co-workers on a lipoprotein characterizing obstructive jaundice indicate, that albumin may participate as an apoprotein in lipoprotein formation. Apolipoprotein A represents the main protein component of HDL. Lipoproteins of density class LDL_2 almost exclusively contain apolipoprotein B. Very-low-density lipoprotenis are characterized by apolipoprotein C in their protein moiety, but contain B-protein in addition.

Evidence for the presence of apolipoprotein A in very-low-density lipoproteins and of apolipoprotein C in high-density-lipoproteins has been given by several investigators (Levy et al. 1966, Alaupovic, 1970).

Biochemical Studies of the $Lp^{(a)}$- Lipoprotein

Introduction: The Lp (a) - lipoprotein, which previously could be determined only by immunological methods, has recently been separated from the accompanying lipoproteins and isolated in a pure state by application of different purification techniques in our laboratory and by Simons et al (1970). It was immunologically characterized as β-lipoprotein but flotation in the ultracentrifuge occurs within the density class of the high density lipoproteins (HDL_2, $1.063 < \delta < 1,125$). The Lp (a)-lipoprotein is distinguished from the β-lipoproteins of the density $1,019 < \delta < 1,063$ (LDL_2) mainly by the following properties:

1. It carries the Lp (a)-antigenic determinants.
2. It has a lower lipid content and a corresponding higher density.
3. It exhibits a slower migration in polyacrylamide gel electrophoresis.

This is possibly due to its higher molecular weight of 5 Mio., reported by Simons et al. These authors also found slightly different aminoacid compositions between both lipoproteins.

However, the similar behaviour of Lp (a)-and LDL_2-lipoproteins in column chromatography on apatit, the coprecipitation with dextransulfate as demonstrated by Harvie and Schulz and the migration in agar immuno-electrophoresis point to a close relation of both these lipoproteins. Most notably the Lp (a)-lipoprotein shows all of the "common β-antigenic determinants" (all except those determinants with group specificity, i. e., Lp, Ag) characteristics for LDL_2-lipoproteins.

In order to study the differences in the molecular structure between the Lp (a)-lipoprotein and other β-lipoproteins, the LDL_2-lipoprotein, which seems most similar to it, was chosen, because a Lp (a)-antithetical gene product is not known and

also is not expected to exist.

For this investigation the respective lipoproteins were treated with proteases and the degradation products studied by comparison. Furthermore the stability of the antigenic determinants against periodate was determined in order to obtain possible information about the chemical nature of the antigenic sites.

Lipoprotein fractions where isolated by ultracentrifugation. Preparation procedure can bee seen in figure 2.

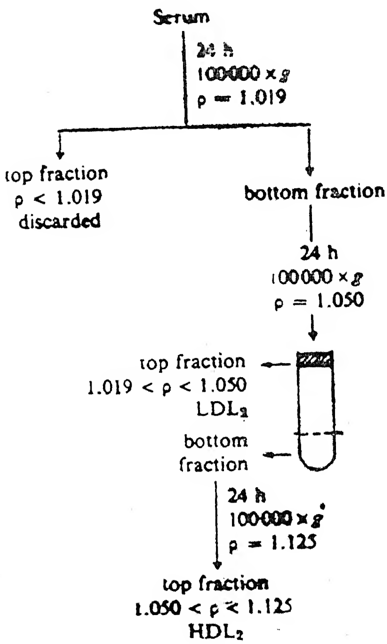

Figure 2

The fractions LDL_2 and HDL_2 were further purified from α_1 lipoprotein and albumin by chromatography on hydroxylapatit as described by Cramer and Bratisten (1961).

Fractions were prestained by sudan-black B. Left Gel LDL_2 fraction, middle Lp (a)-lipoprotein, right α_1-lipoprotein.

Before the enzyme treatment the lipoproteins were transferred into a solution of 1% $(NH_4)_2$ Co_3 by gelfiltration over Sephadex G 25.

Results

Degradation with Trypsin: Lp (a)-lipoprotein and the β-lipoprotein of density class LDL_2 ($1{,}019 < \delta < 1{,}063$) respectively were incubated with trypsin and the reaction products

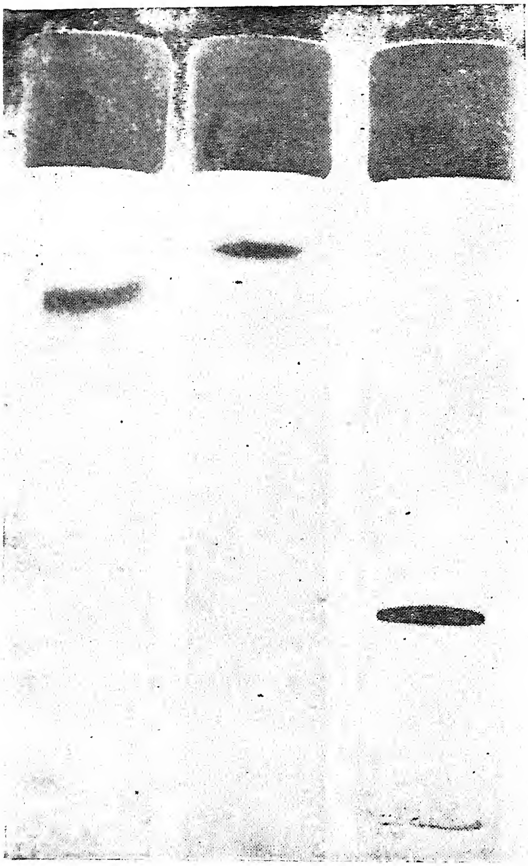

Figure 3
The purified fractions obtained in 3,75% polyacrylamid gels

separated into two fractions by chromatography on Sephadex G 75 (Fig. 4).

The first fraction (T1Lp(a) or T1LDL$_2$) was excluded from the gel, whereas the second fraction (T2Lp(a) or T2LDL$_2$) was retarded and contained smaller tryptic peptides. The elutions pattern from the Sephadex G 75 of the enzyme degradation products from Lp (a)-lipoprotein and from LDL$_2$-lipoprotein resembled

each other qualitatively. A similar elution pattern was also obtained after digestion of both lipoproteins with pronase (fractions P1 and P2). However, a different quantitative distribution of the tryptic fragments into the two fractions was observed: After trypsin incubation of the Lp(a)-lipoprotein ca. 50% of the protein was eluted in the form of oligopeptides in fraction T2Lp(a), whereas the low molecular peptide fragments of LDL_2–lipoprotein amounted only to ca. 20% of the protein. Practically all of the lipoprotein lipids were recoverved in fraction T1Lp (a) or $T1LDL_2$. Fractions T2Lp (a) or $T2LDL_2$ contained less than 1% of the lipid.

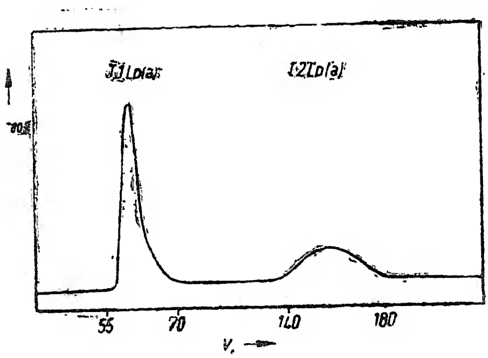

Figure 4

The immunological comparison of native LDL_2-lipoprotein, fraction $TILDL_2$ of the tryptic digestion and $PILDL_2$ of the cleavage with pronase in the Ouchterlony double diffusion-technique showed that all reacted with anti-LDL antiserum but the spur formation between the three probes was indicative for an only partial immunological identity (Fig 5).

This finding could be ascertained by absorption experiments: it was not possible to absorb an anti-LDL antiserum completely by fraction $T1LDL_2$. Such an absorbed antiserum still reacted with native LDL_2-lipoprotein as seen in figure 6.

Similar fraction $PILDL_2$ did not completely absorb an anti-LDL antiserum. It was observed, that $P1LDL_2$– absorbed anti-LDL antiserum reacted not only with native LDL_2–lipoprotein but also with fraction $T1LDL_2$ (figure 7).

However, the anti-LDL antiserum which was absorbed with fraction $T1LDL_2$ formed immunoprecipitates with native LDL_2-lipoprotein only and not with fraction $P1LDL_2$ (figure 8).

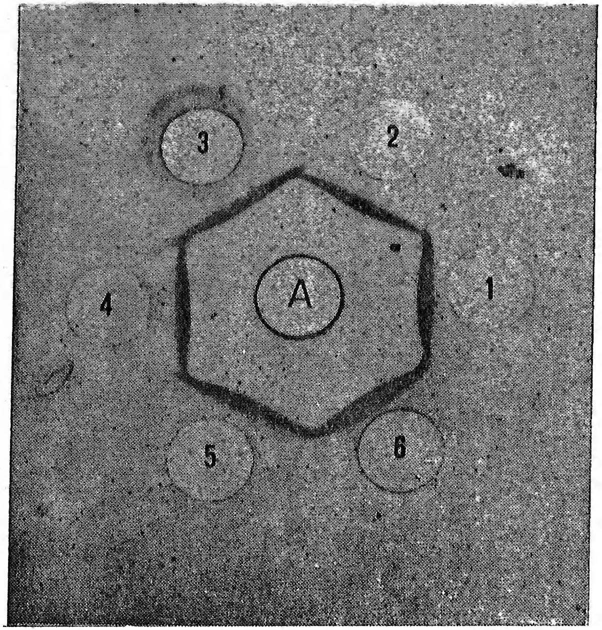

Figure 5: Center well A: Anti-LDL antiserum, wells 1,5,6: different LDL_2–preparations, well 3 : human serum, wells 2,4 : fractions $T1LDL_2$ Note spur formation between LDL_2 and $T1LDL_2$

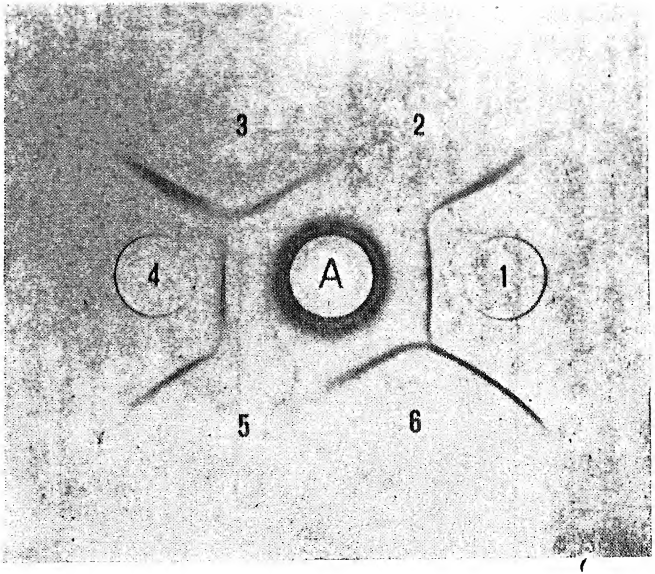

Figure 6: Intra-basin absorption of anti-LDL antiserum by $T1LDL_2$-fraction. Centre well (A): first $T1LDL_2$ followed by anti-LDL antiserum. Wells 1,4: anti-LDL antiserum; wells 3,6: LDL_2; wells 2,5: $T1LDL_2$. Anti-L DL antiserum absorbed by $T1LDL_2$ still reacts with LDL_2 (3,6)

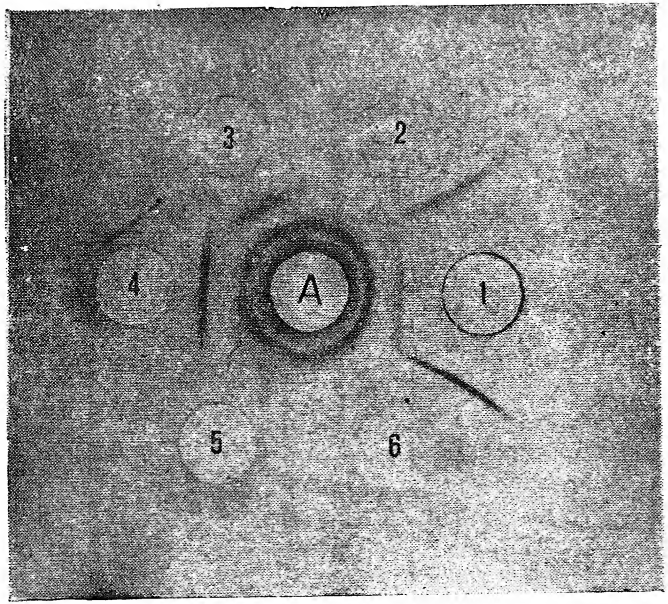

Figure 7 : Intra-basin absorption of anti-LDL antiserum by fraction $P1LDL_2$. Center well (A) : first $P1LDL_2$ followed by anti-LDL antiserum. The absorbed anti-LDL antiserum still retained its reactibity with formation occurred between both precipitates. Unabsorved anti-LDL-antiserum (well 1) reacts with fraction $P1LDL_2$ (well 2,6), while there is no precipitate formation with the $P1LDL_2$–absorbed anti-LDL antiserum

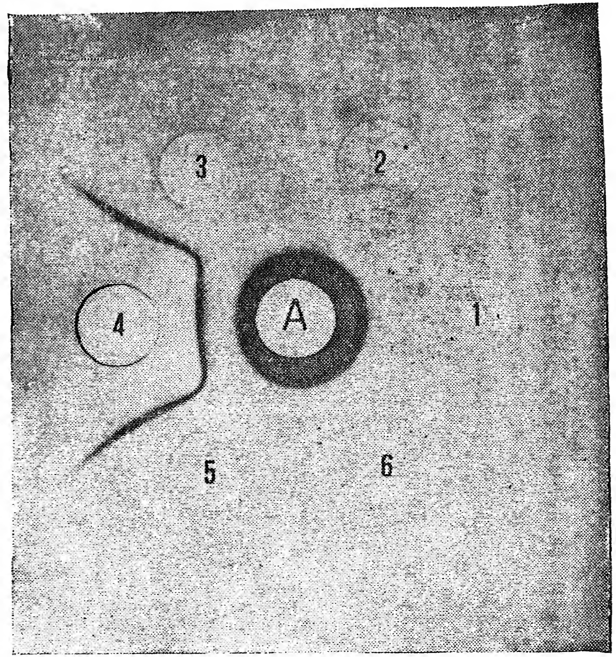

Figure 8 : Intra-basin absorption of anti-LDL antiserum by $T1LDL_2$-fraction. Center well (A) : same as in figure 6. The absorbed anti-LDL antiserum still reacts with native LDL_2 (well 1) and not with the degradation products $T1LDL_2$ (wells 2,5) or fraction $P1LDL_2$ (wells 3,6). Well 4 : anti-LDL antiserum

These results show the existence of three immunologically different LDL-antigen determinants and a decrease of the total number of LDL-antigenic determinants in the order LDL_2-lipoprotein fraction $T1LDL_2$ fraction $P1LDL_2$.

Incubation of Lp (a)-lipoprotein with trypsin or pronase results in a complete loss of immunological Lp (a)-activity (Fig. 9).

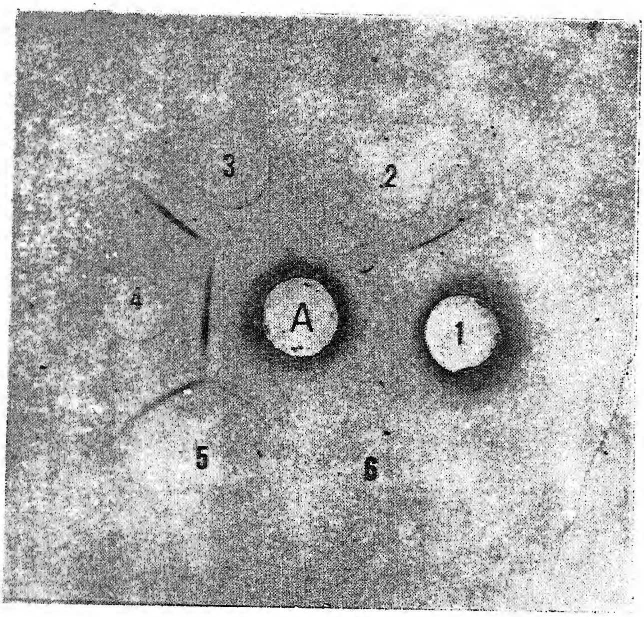

Figure 9

Immunological comparison of Lp (a)–lipoprotein and fraction T1Lp(a).

A : Intra-basin absorption of anti-Lp (a) antiserum by fraction T1Lp (a)

Well 1 : anti-Lp (a) antiserum
Well 4 : anti-LDL antiserum
Wells 2,5 : Lp (a)-lipoprotein
Wells 3,6 : fraction T1 Lp (a)

T1Lp (a) does not precipitate with anti-Lp (a) antiserum, and has lost its ability to absorb anti-Lp (a) antiserum. It still reacts with anti-LDL antiserum and also of part of the "common B-antigenic determinants". The fractions T1Lp (a) and $T1LDL_2$ were found immunologically identical against an anti-LDL antiserum by double diffusion–precipitation

We also could not find any immunological differences between fraction T1Lp (a) and fraction T1LDL$_2$ by means of antisera, which were produced by immunisation of rabbits with either fraction. In the agar gel double diffusion test as well as in the immuno-electrophoresis anti–T1Lp (a) and anti-T1LDL$_2$ antisera reacted specifically with β–lipoprotein. However, in contrast to anti-LDL antisera the anti Tl-fraction antisera could be completely absorbed by use of the lipoprotein-fractions T1. Out of three rabbits, which had been immunized by high doses of fraction T1Lp (a) none showed any antibody formation against the factor Lp (a).

The fractions T2Lp (a) T2LDL$_2$ did not exhibit any reactivity with anti-LDL–or anti–Lp (a)-antisera in the Ouchterlony test.

Disc electrophoresis of Tl-fractions : Well defined and reproducible bands in the gel electrophoresis of the fractions Tl of the tryptic degradation of the lipoproteins were obtained in media, which caused partial or total separation of the lipid from the protein moiety. Fractions T1LDL$_2$, which had been prepared from the sera of several donors showed qualitatively always the same pattern of protein bands in the gel electrophoresis using urea triton × 100–β–mercaptoethanol according to the procedure of Lim. Good separation in the disc-electrophoresis was also achieved with the system phenol-acetic acid-urea according to the method of Takayama. Both fractions, T1Lp(a) and T1LDL$_2$, showed a pattern composed of four major protein bands (figure 10). Thus there were no differences detected between fractions T1Lp(a) and T1LDL$_2$.

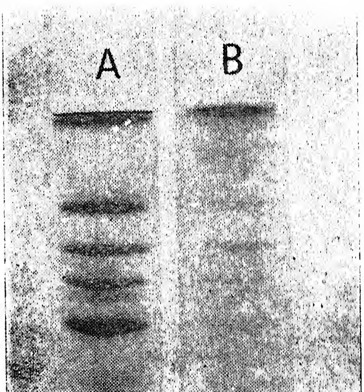

Figure 10

Gel electrophoresis (6% acrylamide). System according to Takayama et al. A: fraction T1LDL$_2$; B: fraction T1Lp (a)

Peptide mapping of fractions T2Lp (a) and T2LDL$_2$: The oligopeptides of the tryptic digests, fractions T2Lp (a) and T2LDL$_2$ which originated from lipoproteins of the same donors were separated two-dimensionally on silica gel thin-layer plates by chromatography followed by high voltage electrophoresis and detected with ninhydrin. Hereby no significant differences of the obtained fingerprints of fractions T2Lp (a) and T2LDL$_2$ could be observed. In order to increase the sensitivity of detection the peptides were reacted with DAN Sylchloride – on fluorescence marker – and the products subjected to two-dimensional thin layer chromatography. Fingerprints of fractions T2Lp (a) and T2LDL$_2$ prepared in this way were very similar to each other. Some seventy different peptide fragments could be recognised (fig. 11). Only two peptide-spots were detected in fraction T2LDL$_2$ (fig. 12). On the other hand in fraction T2LDL$_2$ some peptide-spots did not have their counterpart in fraction T2Lp (a).

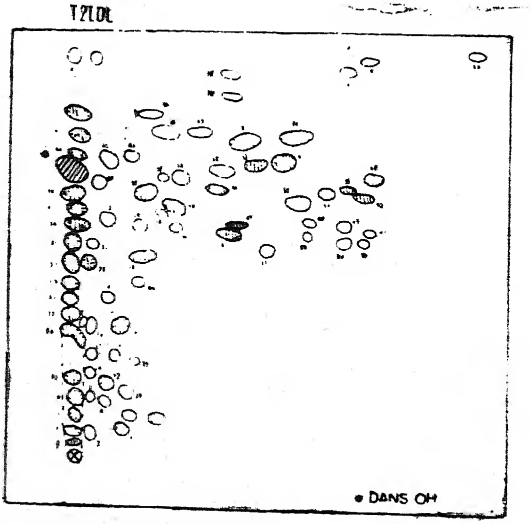

Figure 11

Treatment with periodate: The native lipoproteins, Lp (a)-lipoprotein or LDL$_2$-lipoprotein respectively, were oxydized with periodate. After the reaction the Lp (a-)

lipoprotein had lost its ability to form precipitates with anti-Lp (a) antisera.

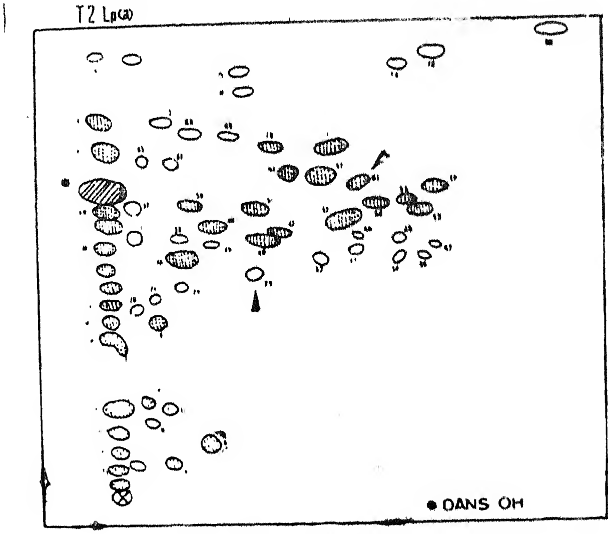

Figure 12

In contrast to this after the treatment with periodate Lp (a)-lipoprotein as well as the LDL_2-lipoprotein had completely retained their reactivity against anti-β-lipoprotein antisera.

Summary and Discussion of Results

Studies of enzymatic degradation of purified native β-lipoproteins were reported by Bernfeld and Kelley (1964), Margolis and Langdon (1966) and Rudman et al. (1968). Bernfeld and Kelley as well as Margolis and Langdon observed, that some 20% of the protein-moiety of native LDL_2-lipoprotein was fractured by tryptic digestion into low molecular peptides. This is in agreement with our results. Bernfeld and Kelley suggest according to their findings, that the proteolytic cleavage by trypsin results in the complete degradation of some of the lipoprotein molecules after which the reaction comes to a halt, because part of the lipid, which is set free, binds to intact lipoprotein thus inhibiting their attack by the enzyme.

On the other hand it was discussed by Margolis and Langdon, that from all β-lipoprotein molecules peptide fragments are cleaved by the enzyme, which are not covered by lipid.

Our findings rather support the suggestion made by Margolis and Langdon. It may be argued, that loss of immunological activity of trypsinized lipoprotein fractions could be caused by masking of the corresponding antigenic determinants by lipid. However, this could not explain our results obtained with gel electrophoresis, where we find the fractions T1Lp (a) and T1LDL$_2$ to show the same pattern of proteinbands. In addition to this, native lipoproteins exhibit a considerably more complicated pattern in the same system of gel electrophoresis as compared to their T1 fractions. Rudman et al, did not observe any change in the immunological properties of trypsin treated β-lipoproteins. This may have been due to an incomplete proteolytic digestion, which is also suggested by the low cleavage of protein (10%) reported by these authors.

The Lp (a)-lipoprotein was fractured into smaller oligopeptides to a much higher degree than the LDL$_2$-lipoprotein. The high molecular fragments from the tryptic degradation, T1Lp (a) and T1LDL$_2$, appear to be very similar to each other. They could neither be differentiated by immunological methods using conventional anti-LDL antisera or sera, which were produced against these fractions, nor by different gel-electrophoretic techniques.

Where as the Lp (a) - immune property was completely lost upon treatment of the lipoprotein with protease, only part of the common β-antigenic determinants were hereby destroyed.

The findings demonstrate, that the major part of Lp (a)-lipoprotein (about 70%) consists of β-Protein.

The higher molecular weight of Lp (a)-lipoprotein as reported by Somins and co-workers and the fact, that there is cleaved a higher amount of peptides from Lp (a)-lipoprotein, may indicate, that there exists a protein component in this lipoprotein, not present in LDL$_2$-lipoprotein.

The Lp (a)-lipoprotein shows a comparably high content of sialic acid (Simons et al).

Degradation of Lp (a)-lipoprotein and LDL_2-lipoprotein by oxidative cleavage with periodate results in a complete loss of Lp (a) - immune property whereas none of the common β-antigenic determinants characteristic for β-protein where hereby destroyed.

These observations may be taken as a possible indication of the carbohydrate nature of the Lp (a) -- antigenic determinant.

Why the differences between LDL -and Lp (a)-lipoproteins cannot be demonstrated in the polypeptide fraction is not yet understood.

A possible explanation would be the glycoprotein - nature of the Lp (a) specifying protein part, because glycopeptides are not expected to be demonstrated by our method of "finger-printing".

Some final remarks concerning the quantitative character of Lp (a)-lipoprotein

Let us come back now to the presumed quantitative character of Lp (a) - lipoprotein.

The different opinions on the specificity of the so called weak Lp (a) - reactions were pointed out till then only by immunological arguments. Now in our laboratory there was available another criterium of characterisation of Lp (a)-lipoprotein. It is different from LDL_2 in its mobility in disc-electrophoresis.

So we applied this technique to look whether a clear alternative division into Lp (a+) and Lp (a—) types could be achieved. For this purpose lipoprotein fractions HDL_2 were prepared by preparative ultracentrifugation. Gel electrophoretic studies of the serum lipoprotein fraction HDL_2 of 35 individuals showed, that using these techniques no clear classification into Lp (a+) and Lp (a—) types could be made. 19 out of 20 sera type Lp (a—) by double diffusion contained in their concentrated HDL_2 fraction a lipoprotein with the electrophoretic mobility characteristic of the Lp (a)-lipoprotein.

This finding may be illustrated by the next figure (Fig. 13)

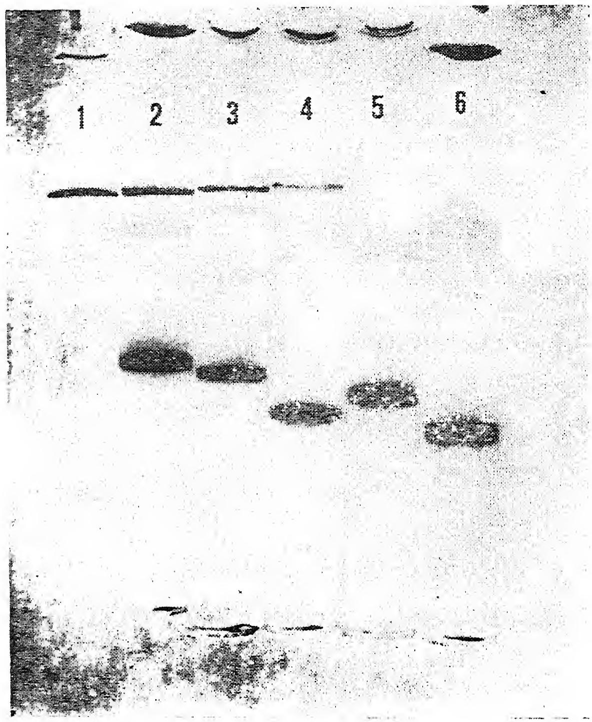

Figure 13

A polyacrylamide gel electrophoresis of a concentrated Lp (a)-fraction (left) and of 5 individual HDL_2-fractions. These were derived from two Lp (a) - positive, one Lp (a) - weak-positive and two Lp (a) - negative donors (from left to right)

Next Figure (Fig. 14) does show 6 further HDL_2-fractions:

This observation confirms previous suggestions, that Lp (a) indeed is a quantitative genetic trait. Especially by this opinion the following observations may be explained as pointed out by Harvie and Schultz:

1. that there is no isoimmunisation against Lp(a)
2. there is no antethetical gene-product known so far

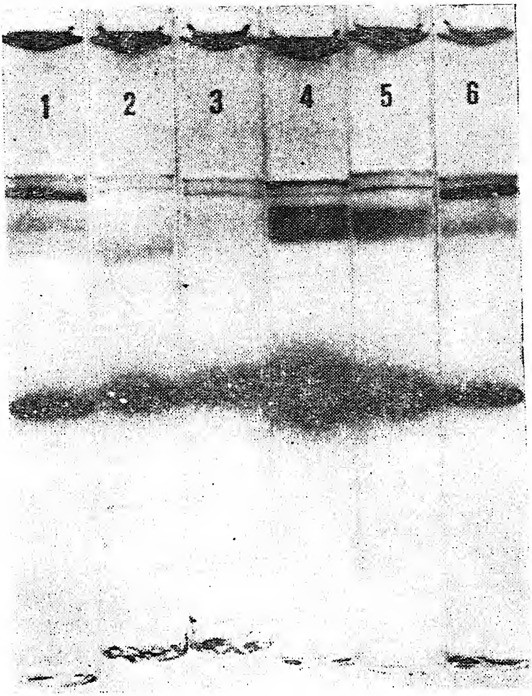

Figure 14

The fast moving bands represent λ_1 - lipoprotein, the slow bands Lp(a)-lipoproteins. The components in between are β-lipoproteins. The corresponding sera were typed from left to right: Lp (a+), Lp (a—), Lp (a—), Lp (a—), Lp (a weak +), Lp (a+).

3. that there have been developed antisera against Lp (a) by immunisation of rabbits with the sera Lp (a—) persons.

NOTES ON THE DISTRIBUTION OF SOME SERUM PROTEIN POLYMORPHISMS IN INDIA

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INTRODUCTION

Since a long anthropologists had developed a strong in, terest in India and on its manifold problems, which she presents to all fields of anthropological research, both cultural anthropology as well as physical anthropology, including human genetics. Thus already in the 19th century a good number of physical anthropological field work were undertaken done in India, by anthropologists like Dalton, the Sarasins, Shortt, Foyer, Fawcett, Jagor, Lapicque, Thurston and Emil Schmidt. Though these previous investigations could not satisfy modern requirements, they yielded, however, first informations on the anthropological structure of the Indians. And furthermore, these previous anthropological studies induced without any doubt the much more comprehensive anthropological research in India, carried out by Risley (1915), V. Eickstedt (1934), Guha (1935), Mahalanobis (1949) and Gupta and Dutta (1966). Basing on the data obtained by these and numerous other workers in this field, problems of the taxonomic classification, the origin and the racial history of the Indians could be discussed and solved partly.

Nowadays a good number of Indian research groups are quite successfully working on the anthropological problems of their country. They have not only enlarged the methodological basis of their research (adding i. e. dermatoglyphics, P.T.C.-tasting and blood groups typing to anthreo pometric measurements), but also the formulation of thir-

research questions, because problems of modern human population genetics such as genetical effects of inbreeding or the effects of natural selection on the population structure have been more and more taken into consideration during the last years. This shows, that the anthropological research in India – like in other countries – is turning more and more from a preponderant descriptive into an analytical stage.

Whilst referring to the distribution of anthropometric and dermatoglyphic traits in India comprehensive data are available. our knowledge of the distribution of serological traits (blood groups, serum protein groups, enzyme groups, haemoglobin variants) in India is rather limited. This is in a highest degree regrettable, as in modern anthropology all these traits proved to be highly important, namely for the genetical description of human populations as well as for the evaluation of those factors, which influence evolutionary processes in man. Most of our informations on the frequency and distribution of the various blood group systems in India could be summarized already by Mourant (1954, 1958) and Walter (1962), and since that time only a few new data came up. From these data only a very coarse pattern of the ABO blood group distribution in India could be obtained, and particularly in respect of the blood group polymorphisms P, Kell, Duffy, MN, Ss, Rhesus etc. our informations are very small. The same is valid with respect to the enzyme groups, and its incidence in India which is up to now only known by a few studies in North India (Singh, unpubl.), Madras and Bengal (Das et al, 1970), while our knowledge on incidence and distribution of haemoglobin variants is fairly better (Livingstone 1967). More data on blood and enzyme group polymorphisms in India are therefore desirable in order to learn their geographical distribution patterns and to exhaust their anthropological contents.

In this paper the significance of some serum protein polymorphisms for the anthropological research of India will be discussed, namely the haptoglobins, the Gc proteins, the transferrins, the ceruloplasmins, the β_2-glycoprotein I system and the Pi (= protease inhibitor) system. Though the number of

hitherto tested Indian populations is rather small, some anthropological notes on their occurrence seem to be possible already, which may stimulate further research in this field.

Haptoglobin System

The haptoglobin polymorphism consists of three phenotypes – Hp 1 – 1, Hp 2–1, Hp 2–2 –, which are controlled by two auto somal allelic genes : Hp^1 and Hp^2. It can be demonstrated by starch gel electrophoresis (Fig. 1). After the discovery of this genetical polymorphism by Smithies and Walker (1956), it could be shown, that so called haptoglobin – subtypes are existing (Connell et al, 1962), to which we refer later on. The

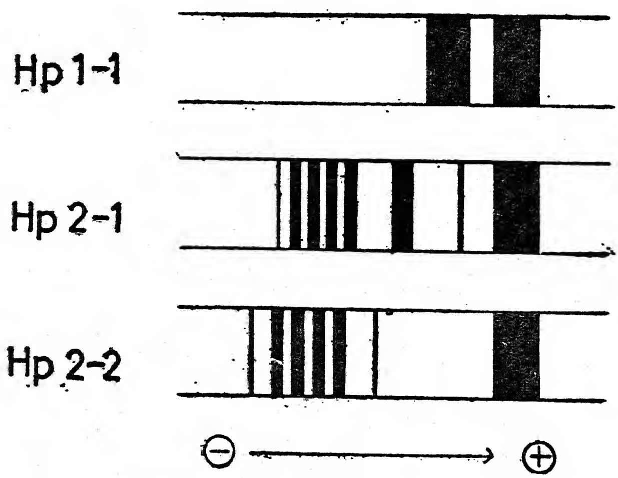

Figure 1

Haptoglobin phenotypes

world distribution of the haptoglobin alleles reveals a marked geographical distribution in homogeneity, characterized by generally high Hp^1-frequencies in Europe, America, Africa Australia, but also in South West Asia (Iran, Pakistan). Against that Indians are striking by high Hp^2–, but low Hp^1-

frequencies (Fig. 2). This is characteristic for all hitherto tested Indian populations: Tamils, Irulas, Kurumbas, Oraons (Kirk and Lai 1961), Bengalis and Punjabis (Tiwari 1960, 1961), Brahamins, Rajputs, Doms and Tharus from the Kumaon

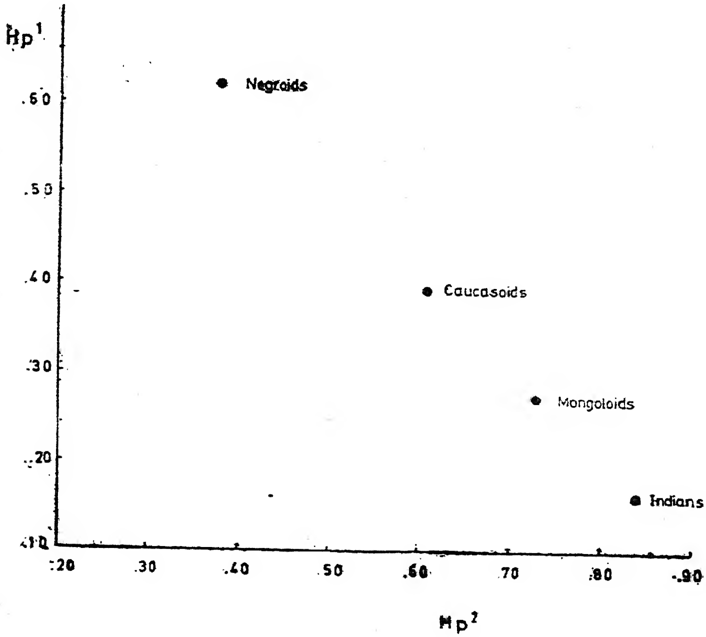

Figure 2

Distribution of haptoglobin alleles in Negroids, Caucasoids, Mongoloids and Indians

region in North India (Chopra 1970) and a population sample from West Bengal tested by ourselves (Walter et al, unpublished). In all these population samples the frequency of Hp^1-alleles varies from 0.09 (Tamils) to 0.22 (Tharus), resp. that of Hp^2-alleles from 0.91 – 0.78. Overlooking these data it surprises, that the Hp^2-frequency seems to increase from north towards south. This supposed distribution gradient must be established, however, by further research.

The only exception regarding the distribution of haptoglobin alleles in India is represented by the Todas, in which

the Hp^1-frequency was found to be 0.37, whereas the Hp^2-frequency comes to 0.63. As the Todas, living in the South Indian Nilgiri Hills, are a rather small group and differ physically and culturally from the surrounding South Indian populations, it has been supposed (Kirk and Lai 1961), that their discrepant Hp allele distribution may reflect a remote origin, genetic drift, or a combination of both. Rivers (1906) and V. Eickstedt (1934) presume a northern origin of the Todas, who settled in the relatively cool biotops of the Nilgiri Hills and were more or less biologically isolated from their neighbours for many centuries, perhaps even several thousands of years. Basing on these premises it seems to be quite admissible, that the high frequency of Hp^1 alleles in the Todas was brought at their settlement in the Nilgiri Hills and could maintain due to lacking or restricted biological contacts with neighbouring populatlons, and possibly also by some selective advantage of the Hp^1 alleles under the environmental conditions of the Nilgiri Hills. Genetic drift might have increased this effect. It seems desirable to reinvestigate this problem, on a wide anthropological basis and in consideration of as much genetical markers as possible.

Apart from the Todas all Indians are characterised by high Hp^2-frequencies, the highest in all the world. Basing on this undoubted fact the cradle of this haptoglobin allele has been placed in India (Bearn and Parker 1965). It is most likely, that the Hp^2-allele resulted from a non-homologous exchange between two Hp^1-alleles, Hp^{1f} and Hp^{1s} (Smithies et al, 1962). Such an occurrence must have been happened repeatedly in the history of the human species, for there are no solid anthropological arguments present to assume a spreading of Hp^2-alleles from India all over the world. But the extraordinarily high frequencies of Hp^2-alleles in India must be caused by a particular selective advantage of this allele under the living conditions of this geographic area. How far haemolytic diseases as in malaria may play a role in this connection must remain an open question and requires further research (Walter and Steegmüller 1969). In this context it may be mentioned, that no associations are existing between haptoglobin types and leprosy, as could be recently demonstrated in a sample from West Bengal

(Walter et al, unpubl.). Supposed associations between haptoglobin types and typhoid antibody response require further research, before a possible selective significance of these associations can be taken into consideration. It seems to us, that these above mentioned presumed associations, found by Nevo and Sutton (1968), are of highest interest particularly regarding the distribution of haptoglobin phenotypes and alleles in India, as it could be demonstrated, that individuals, who are Hp 2–2 had higher typhoid anti - O titers (mean = 5.41) after immunization than individuals who are Hp 1 – 1 (mean = 5.03) or Hp 2 – 1 (mean = 4.87). It would be very interesting therefore to tackle this problem on Indian materials.

As far as I know haptoglobin-subtypings on Indians have been hitherto done only on a small sample (n=85) from Bombay (Shim and Bearn 1964). In this sample the frequency of Hp^{1f}-alleles comes to 0.05, that of Hp^{1s} to 0.10. Though these data are without any doubt too small as to permit detailed anthropological conclusions, they correspond to those obtained on other Asiatic populations. According to the review given by Kirk (1968) all Asiatic populations are characterised by very low or even lacking Hp^{1f}-frequencies, whereas this allele occurs in European or African populations in much higher frequencies: Europe 0.14 – 0.31, Africa ~0.50 However, more data from India as well as from other parts of the world, are required to get to know the exact geographical distribution pattern of the haptoglobin subtypes and the alleles controlling them.

Gc System

The Gc serum protein polymorphism has been discovered by Hirschfeld (1959). It consists of three phenotypes – Gc 1–1, Gc 2-1, Gc 2–2 –, which are controlled by two autosomal allelic genes: Gc^1 and Gc^2. The demonstration of this polymorphism is performed by means of immunoelectrophoresis (Fig. 3). Up to now the number of Gc typed Indian populations is rather small. Informations are available from Kirk, Cleve and Bearn (1963), who tested Indians from Malaya, Oraons, Irūlas and Kurumbas, from Chopra (1970), who tested four samples from the North Indian Kumaon region (Brahmins, Rajputs, Doms and Tharus), and from ourselves, namely

a sample from West Bengal (Walter et al unpublished). The Gc allele frequencies do not differ very much between these

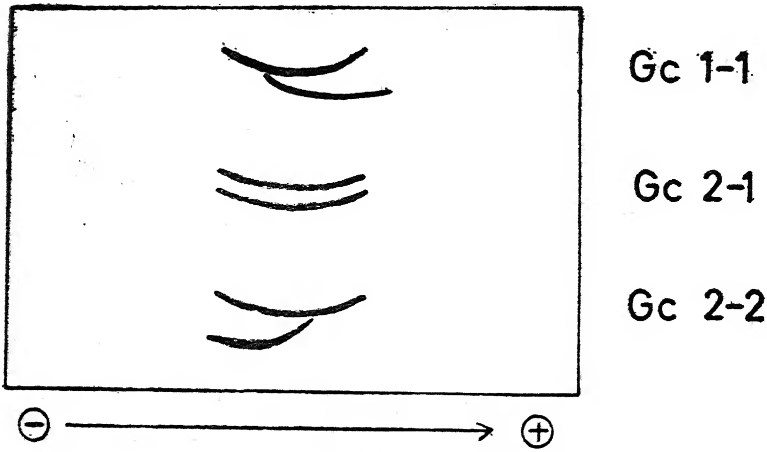

Figure 3
Gc phenotypes

population samples : the frequency of Gc^1 alleles varies from 0.644 (Kurumbas) to 0.760 (West Bengal), that of Gc^2 alleles from 0.356 to 0.240. Different from these values are the Irulas, in which Gc^1-frequencies come to 0.902 ($Gc^2 = 0.098$). However, as this sample is very small (n=61), this difference may be due to chance. In any case more and detailed studies on the distribution of Gc phenotypes and its alleles are necessary to know the exact geographical distribution pattern in India.

Comparing the available known Gc allele frequencies of Indians to those of Caucasoids, Mongoloids and Negroids, a clear resemblance between Indians, Caucasoids and Mongoloids is remarkable (Fig. 4). All these groups are characterised by obviously high Gc^2 and low Gc^1 frequencies, while Negroids are striking by high Gc^1 and low Gc^2 frequencies. However, a satisfactory interpretation of these findings is still not possible, as the physiological function of Gc proteins is unknown. In this connection, however, it has to be mentioned, that Nevo and Sutton (1968) found some associations between Gc phenotypes and typhoid antibody response. Individuals showing the heterozygous Gc 2-1 phenotype were striking by

higher typhoid anti –O titers (mean=5.61) after immunization than Gc 1–1 (mean=4.86) or Gc 2–1 (mean=4.92) ones. How

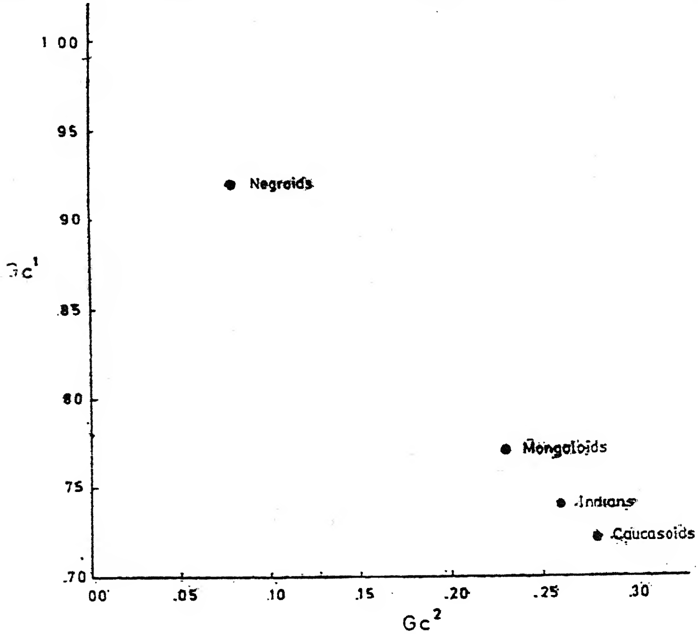

Figure 4
Distribution of Gc alleles in Negroids, Caucasoids, Mongoloids and Indians

far these associations are of selective significance must be clarified by further research. Another interesting association between Gc phenotypes and disease could be pointed out by ourselves (Walter et al, unpublished). Comparing the Gc phenotype distribution in a sample of leprous individuals from West Bengal to the healthy ones (Table 1), it could be

TABLE 1

Gc Phenotype and Allele Distribution in Leprous and Healthy Indians

		Gc Phenotypes (%)				
	n	1–1	2–1	2–2	gc^1	gc^2
Leprous	599	63,3	29,0	7,7	0.778	0.222
Healthy	384	55,5	35,7	8,8	0.733	0.267
Total	983	60,2	31,6	8,2	0.760	0.240

$x^2(2)=6{,}012$; $0{,}05>P>0{,}02$

demonstrated that in leprous individuals the incidence of Gc 1–1 phenotypes is much higher, where as the incidence of Gc 2–1 phenotypes is much lower as compared to healthy persons. These differences are significant at least on 5% level and confirm similar results obtained by Spielmann et al (1970), on Negroes from Eastern Africa. Much more research will be necessary, however, to establish these associations and to elucidate their possible selective significance.

Transferrin System

The existence of a genetically controlled transferrin polymorphism has been first reported by Smithies (1957). Up to now at least 28 transferrin variants have been published, which are supposed to be controlled by at least 18 autosomal allelic genes (Fig. 5). Using starch gel electrophoresis the common Tf types (Tf C) as well as the fast (Tf B) and slow moving ones (Tf D) can be typed without any difficulties, whereas the exact identification of the various Tf variants within the classes of fast or slow mobility is quite problematically. In our opinion such identifications are only possible by means of peptide analysis as has been performed successfully by Wang et al (1965, 1966, 1967). Because of these methodological difficulties it seems to be convenient at the moment to discuss only the distribution of fast, common and slow Tf variants, omitting the proposed subtypes. So we proceed for a recently published study on the world distribution of Tf phenotypes and alleles (Walter and Bajatzadeh 1971).

Transferrin typings on Indian populations so far reported are very rare. Informations are only available from Tamils, Todas, Irulas, Kurumbas, Oraons (Kirk and Lai 1961), Bengalis (Tiwari 1960), Brahmins, Rajputs, Doms and Tharus from the North Indian Kumaon region (collected by Dr. V. P. Chopra) and West Bengal (Walter et al, unpublished). From these population samples it is to be seen, that the frequency of the various Tf variants within India seems to be very low. The mean frequency of Tf^c alleles comes to 0.971, whereas that of Tf^b and Tf^d alleles are much lower: 0.001 resp. 0.008. How far the distribution of Tf^c alleles within India is characterised by a distinct geographical distribution pattern, which would

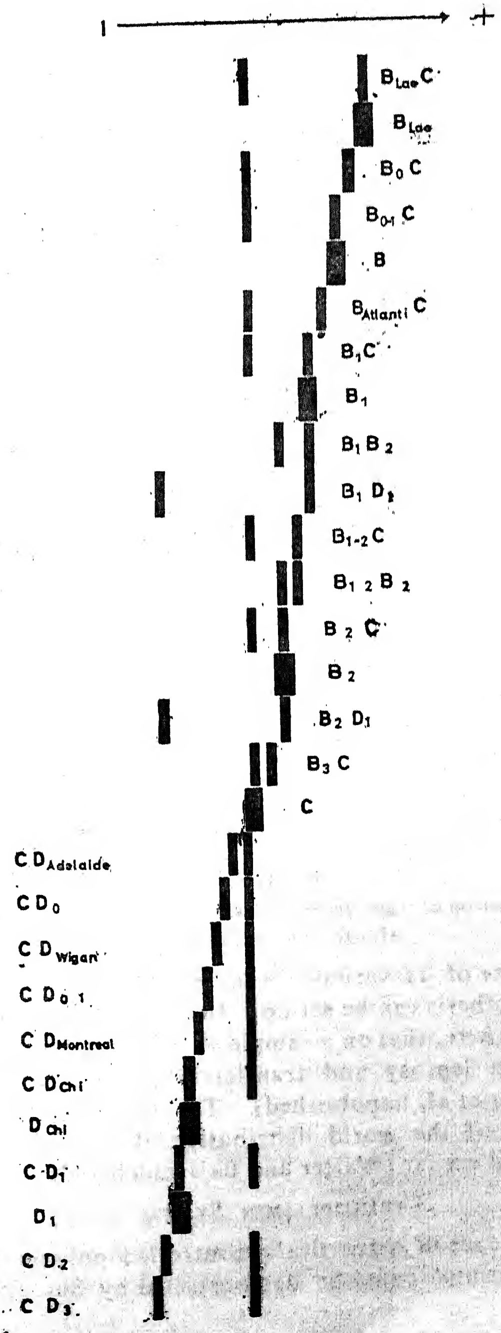

Figure 5: Transferrin phenotypes

allow particular anthropological conclusions, cannot be demonstrated at the moment. More and detailed studies are therefore urgently required.

Comparing the average Indian Tf allele frequencies to those of Caucasoids, Mongoloids and Negroids (Fig. 6), it is to be seen that Indians are very similar to Caucasoids, namely by high Tf^c and low Tf^d frequencies, while they differ obviously from Mongoloids and especially from Negroids, who are striking by much higher Tf^d frequencies. More informations on

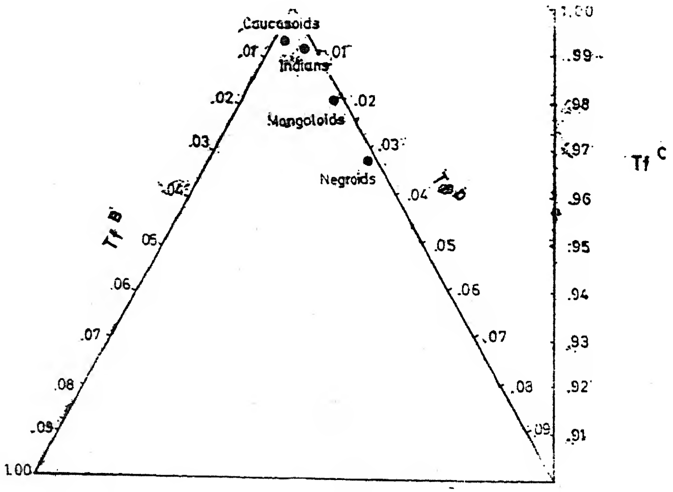

Figure 6
Distribution of transferrin alleles in Negroids, Caucasoids, Mongoloids and Indians

the occurrence of Tf variants in India are necessary, however, before a hypothesis can be set up. In addition to it, it should be mentioned here, that on a sample of West Bengal no associations between leprosy and transferrin phenotypes could be found (Walter et al, unpublished). The question of the non-homogeneity of the world distribution of the Tf alleles has been discussed earliar (Walter and Bajatzadeh 1971).

Ceruloplasmin System

The existence of a genetically controlled polymorphism of the ceruloplasmins could be demonstrated by Shreffler et al,

(1967, 1968). On the basis of family studies they assumed the existence of three autosomal allelic genes: Cp^a, Cp^b, and Cp^c, determining six phenotypes: Cp A, Cp B, Cp C, Cp AB, Cp AC, Cp BC. Some more phenotypes were reported by Shokeir et al (1967, 1968). All these Cp phenotypes are demonstrated by means of starch gel electrophoresis (Fig. 7.)

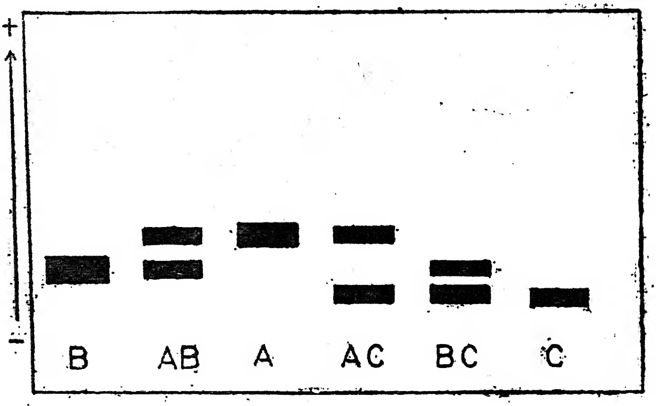

Figure 7

Ceruloplasmin Phenotypes

Typing of the ceruloplasmin variants on Indians have been done only on the Kumaon sample from Chopra (1970) and on our sample from West Bengal (unpubl.). In the Kumaon region the observed phenotype frequencies were: Cp AB=2, 4%, Cp B= 97,6% (n=341): the corresponding values in the West Bengal sample were: Cp AB=2,5%, Cp B=97,2%, Cp BC= 0,3% (n=978). The gene frequencies obtained from these data amount to Cp^a=0.012, Cp^b=0.988 in the Kumaon region and Cp^a=0.012, Cp^b=0.986, Cp^c=0.002 in West Bengal. These figures do not reveal any marked differences between these two Indian samples.

Comparisons of the known Cp allele frequencies of Indians with that of Caucasoids, Mongoloids and Negroids show an obvious resemblance between Indians, Caucasoids and Mongoloids, who differ considerably from Negroids, particularly by much lower frequencies of Cp^a and higher frequencies

of Cp^b alleles (Fig. 8). The anthropological significance of this observation can still not be understood, particularly because, comprehensive ceruloplasmin typings on Indians as well as on Mongoloids are yet to come. But as our findings seem to be of some anthropological interest, they should be mentioned here. It would be welcomed, if they could stimulate further

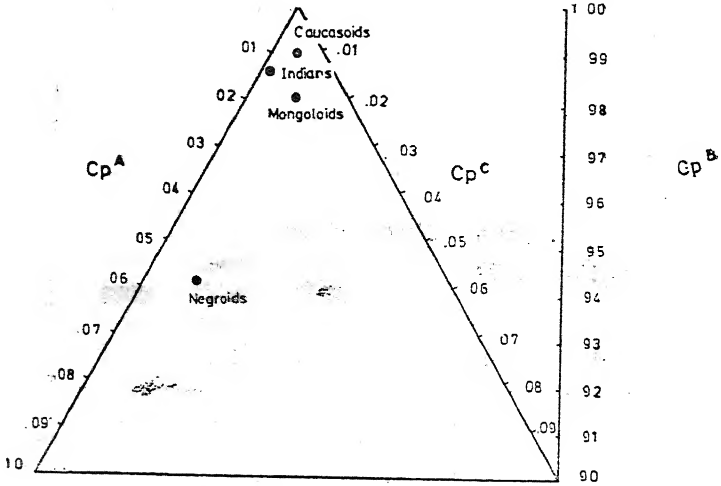

Figure 8

Distribution of ceruloplasmin alleles in Negroids, Caucasoids, Mongoloids and Indians

research on this topic. It should be mentioned still that no association between leprosy and ceruloplasmin phenotypes could be found on our West Bengal sample (Walter, unpubl.).

β_2-Glycoprotein I System

Though the concentration of β_2- glycoprotein I in serum is influenced by factors like age, diseases (i.e. chronic liver diseases such as severe liver cirrhosis), and pregnancy, Cleve (1968) has shown, that the individual concentration of this protein is also controlled by genetic factors. In 94% of sera the concentration varies from 16 – 30 mg/ 100 ml with a mean value of 21.3 ± 3.6 mg/ 100 ml. Lower concentrations were found in 6% of the sera: $\bar{x} = 10.0 \pm 1.3$ mg/ 100 ml. The results of family studies

by Cleve (1968) and Koppe et al (1970) suggested that these concentrations are controlled by a pair of autosomal co-dominant alleles: Bg^n and Bg^d. Individuals homozygous for the common allele Bg^n were found to have β_2-glycoprotein I levels between 16 and 3o mg/ 100 ml, heterozygous ones (Bg^n/Bg^d) between 6 and 14 mg/ 100 ml. Individuals homozygous for the allele Bg^d show deficiency of β_2- glycoprotein I (less than 5 mg/ 100ml). The demonstration of the β_2- glycoprotein I phenotypes is carried out by means of the radial immunodiffusion technique as described by Mancini et al (1963).

Our present knowledge of the distribution of β_2- glycoprotein I phenotypes and alleles in India is restricted only to two population samples, one from the Kumaon region, the other from West Bengal. Between these two samples no differences could be demonstrated, as they reveal nearly equal phenotype and allele distributions, namely in the Kumaon region: Bg N-N=90,8%, Bg N-D=9,2%, Bg D-D=0,0%: Bg^n=0.954, Bg^d=0.046 (n=108), and in West Bengal: Bg N-N=90,8%, Bg^n N-D=9,1%, Bg D-D=0,1%: Bg^n=0.954, Bg^d=0.046 (n=964).

Comparing these frequencies to that of Caucasoids, Mongoloids and Negroids (Fig. 9), it is to be seen, that Indians are quite similar to Caucasoids, while they differ obviously from Mongoloids and Negroids, namely by a lower frequency of the Bg^d allele and a higher frequency of Bg^n. Much more β_2- glycoprotein I typings from Indians as well as from Mongoloids and Negroids are necessary, however, to establish these findings and to draw reasonable anthropological conclusions. It should be added, that our material from West Bengal revealed no differences in the distribution of β_2- glycoprotein I phenotypes between leprous and healthy individuals.

Pi System

The last serum protein polymorphism we are discussing here is the so-called Pi-system (= protease inhibitor). It has been discovered by Fagerhol and Braend (1965) and comprises at least 20 different phenotypes, which are controlled by at least

nine autosomal allelic genes. The demonstration of this system is

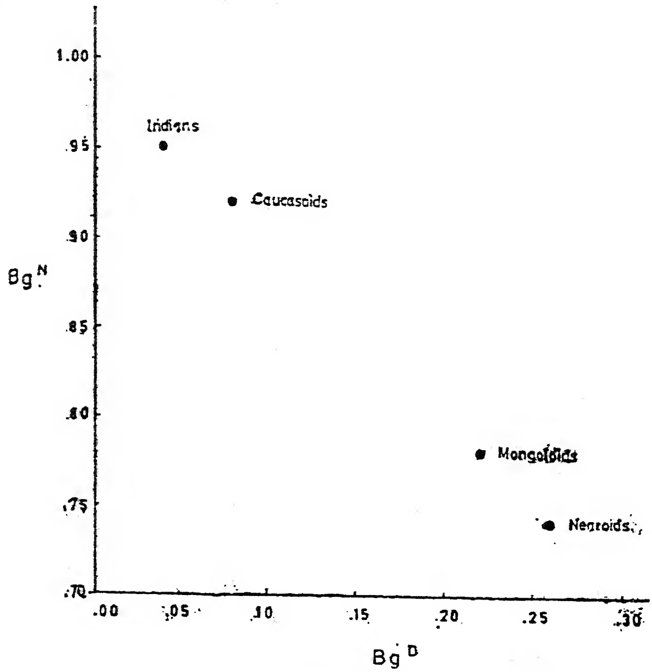

Figure 9

Distribution of β_2-glycoprotein I alleles in Negroids, Caucasoids, Mongoloids and Indians

possible by means of starch gel electrophoresis (Fig. 10) Except the Pi^m allele the occurrence of all the other alleles is generally low (Kellermann and Walter 1970).

From India up to now only two samples could be tested for Pi phenotypes: one sample from the Kumaon region and one from West Bengal. They do differ somewhat in the frequencies of the various Pi phenotypes, but these differences are likely due to chance. Thus in the Kumaon region (n=430) the following allele distribution is present: $Pi^m=0.994$, $Pi^z=0.006$, whereas in West Bengal (n=982) the allele frequencies come to: $Pi^m=0.990$, $Pi^z=0.001$, $Pi^x=0.006$, $Pi^f=0.001$, $Pi^s=0.001$, $Pi^l=0.001$.

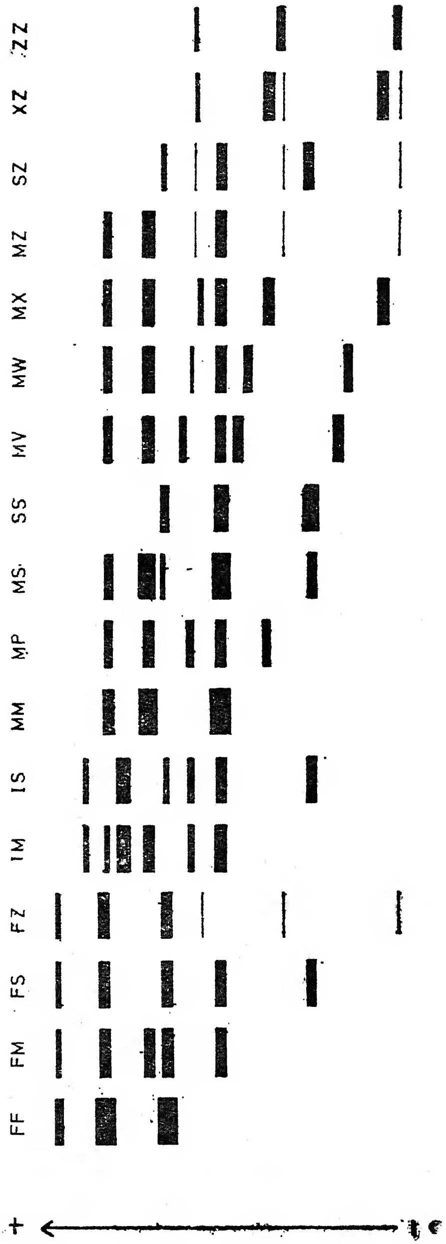

Figure 10: Pi phenotypes

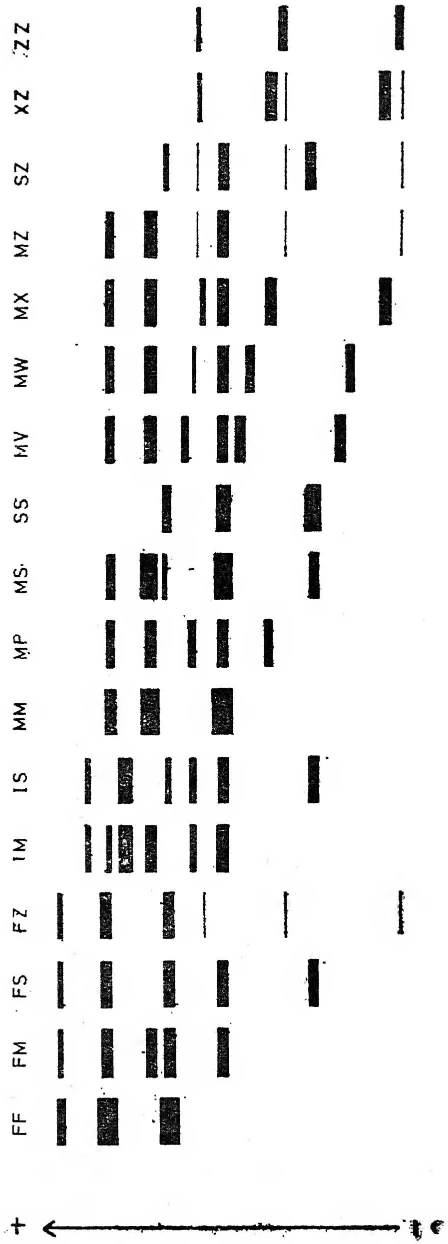

Figure 10: Pi phenotypes

variability of the various serum protein polymorphisms within India are possible. Much more research therefore is necessary to know the detailed distribution patterns of the polymorphisms, which have been considered here. It seems to me, that this will be one of the most important problems for the study of the physical anthropology in India. These will no doubt enable us to solve a good number of open anthropological questions, especially with regard to those factors, which are influencing the genetical make up of human populations (malaria, typhoid fever etc.). The available known Indian gene frequencies concerning the serum protein polymorphisms Hp, Gc, Tf, Cp, β_2-glycoprotein I and Pi have been summarized in Table 2 and have been compared with the corresponding data of Caucasoids,

TABLE 2

Comparison of the Mean Gene Frequencies of Six Serum Protein Polymorphisms in Indians, Caucasoids, Mongoloids and Negroids

	Indians	Caucasoids	Mongoloids	Negroids
Hp^1	0.164	0.384	0.267	0.619
Hp^2	0.836	0.616	0.733	0.381
Gc^1	0.738	0.723	0.774	0.918
Gc^2	0.262	0.277	0.226	0.082
Tf^c	0.991	0.993	0.981	0.967
Tf^b	0.001	0.004	0.001	0.001
Tf^d	0.008	0.003	0.018	0.032
Cp^a	0.012	0.008	0.009	0.045
Cp^b	0.986	0.991	0.978	0.946
Cp^c	0.002	0.001	0.013	0.009
Bg^n	0.954	0.937	0.780	0.742
Bg^d	0.046	0.063	0.220	0.258
Pi^m	0.997	0.907	0.994	0.982
Pi^f	0.001	0.051	—	0.016
Pi^s	0.001	0.031	—	0.002
Pi^z	0.001	0.011	0.006	—

Mongoloids and Negroids. From this table it has to be seen, that in general the Indian frequencies are quite similar to

Caucasoid and Mongoloid ones, while they differ considerably from the Negroid frequencies. This comes also clear from Table 3, in which the genetic distances are given, which have been calculated according to the formula presented by Cavalli-Sforza et al (1969). One may conclude from these values, which of course must be evaluated very cautiously, that the life condition of Negroids are quite different from that of the other groups, causing for that reason a quite different genetic situation, which is expressed by the obviously high genetic distance values. Our informations with regards to the distribution of genes pertaining to all the serum protein polymorphisms must be supplemented with additional data from all the population groups of the world especially from Indian population groups so as to enable us to undertake a detailed comparison and to establish a hypothesis.

TABLE 3

Genetic distances. Based on the mean gene frequencies in six serum protein polymorphisms (Haptoglobin, Gc, transferrin, ceruloplasmin, β_2–glycoprotein I, Pi)

	Indians	Caucasoids	Mongoloids	Negroids
Indians	—	0.163	0.143	0.292
Caucasoids		—	0.186	0.236
Mongoloids			—	0.229
Negroids				—

SUMMARY

The so far known distribution of genes and phenotypes of the serum protein polymorphisms Hp, Gc, Tf, Cp, β_2– glycoprotein I and Pi within India is reviewed. Though the up to now present data are rather small, they indicate certain homogeneity within this country, which should be further analysed by more and comprehensive research. Comparing the hitherto Indian data to that from Caucasoids, Mongoloids and Negroids a striking general resemblance to Caucasoids, and Mongoloids is to be seen, whereas Indians differ considerably from Negroids. It would be welcomed, if henceforth serum protein group

typings would be performed on a much bigger scale than so far. The exact knowledge on the geographical distribution patterns of the various serum protein polymorphisms would allow us to discuss a great number of physical anthropological questions. not at last such of analytical population genetics. It would be welcomed, if these notes could stimulate some research work on this topic.

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PALMAR CREASES AND SCHIZOPHRENIA

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INTRODUCTION

The growing development and utility of palmar flexion creases and palmar dermatoglyphics in Anthropology, Human Biology and Medical Genetics has fully been recognised. While definite progress in genetics of palmar flexion creases remains yet to be accomplished. Biswas (1966) stated that "since the discovery of trisomy as the cause of mongolism, dermatoglyphic analysis have given way to chromosomal investigations as a diagnostic procedure. Nevertheless, the science of dermatoglyphics remains important for quick screening of infants suspected of trisomy and for confirmation of clinical diagnosis when chromosomal investigations are not possible."

In understanding certain, medical syndromes dermatoglyphics has served as a valuable tool. Bonnevie (1924), in the study of embryology, has established a constant parallelism between dermal configurations and the dermal nerves. It follows that through embryonal variations of papillary nerves, transmissible characteristics are expressed in the papillary patterns determined in their genesis and that "these patterns are conclusive indices of inherent traits of characters".

In considering the skin embryologically, Pall and Blumel (1928) contend that the tissue which is folded in the cerebrum forming convolutions and that which is folded in the skin producing furrows and crests, have the same origin. The authors further tried to establish correlation between brain and dermal configurations. As a matter of fact the whole nervous system, brain, spinal cord and peripheral nerves, originates from a common germinal layer (ectoderm). The connection between Palmar flexion creases and mental disorder is quite logical and provides an obvious field for future work.

The central problem here is whether persons affected with certain diseases are distinguished from the non-diseased by characteristics of palmar flexion creases.

Schizophrenia is a mental disease in which manifestations of split personality are prominent. Poll (1935) in course of his study on Schizophrenic patients and dermatoglyphics gave a relationship between finger prints and the disease. Later Moller (1935) confirmed Poll's (1935) observation. A similar study of Duis (1937) indicates that the sex difference is the same as in the normal population. Inconsistently, he regards the Schizophrenics as showing no special distinction in total frequencies of patterns in the face of data which agree with Poll and Moller. Raphel and Raphel (1962) hold nearly the same view in their study of finger prints of 100 Schizophrenic patients.

Biswas and Bardhan (1966) provided recent work on palm prints and Schizophrenia. Besides the study of main line terminations and frequencies of axial triradii among the patients and control group they have also observed the presence of pearl line and the simian crease.

As far as the review goes, it seems that no comprehensive work has been done in the direction of Palmar creases and diseases. According to Lestrange (1969) and Sarkar (1961), the application of palmar flexion creases in complex population problems has always yielded negative results, they advocating the need for more sensitive methods of analysis. The author while agreeing with Lestrange, wishes to add that even the most sensitive method of analysis could not be really effective unless supported by accurate means of formulations of palmar flexion creases. The method of crease formulations by Bali and Chaube (1971) eliminates the possibility of genetic diversity between various creases. In the present study genetic parity of palmar creases among the schizophrenic patients and the normal individuals (control group) has been worked out.

Material and Method

In the present study, total sample is constituted of bilateral palmar prints of 90 male schizophrenic patients who are hospitalised in the mental Hospital Central Jail of Delhi, and

have been compared with normal man of the same racial stock. The patients belonged to the high castes and are of Punjabi origin. No caste and sub-caste division have been done for the small number of sample.

Bali and Chaube (1971) classified the main flexion creases into the following: (a) distal transverse crease (b) proximal transverse crease and (c) radial longitudinal crease, on the basis of having common point of distinction, i.e., their point of origin. It could also be seen that most of the creases emerge from the region occupied by the interdigital pad I referred to as the "Radial base point". On the basis of this trait the palmar creases could be classified into three main categories (Fig. 1):

Single radial base crease (SRBC)
Double radial base crease (DRBC)
Triple radial base crease (TRBC)

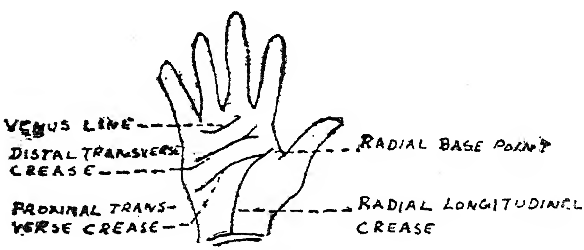

Figure 1
Palmar Crease

This three-fold classification signifies the base point of crease origin that is when creases originate from a single base point on the radial side are called single radial base creases, when originate from the double base points on the radial side are called double radial base creases and when originate from the triple base points are called triple radial base creases, thus eliminating the need for keeping simian crease as the land mark of crease classification of the palm.

The double radial base crease could further be divided into two groups on the basis of its distal and proximal position.

The finer classification of these principle types is based upon the initial split or bifurcation of the transverse crease. If the split is radial ward, starting from the ulnar end, the sub-types could be numbered according to the position of the splitting point (Fig. 2, S_1, S_2, S_3) with regard to the digit of the hand. Double radial base creases have also been subdivided in

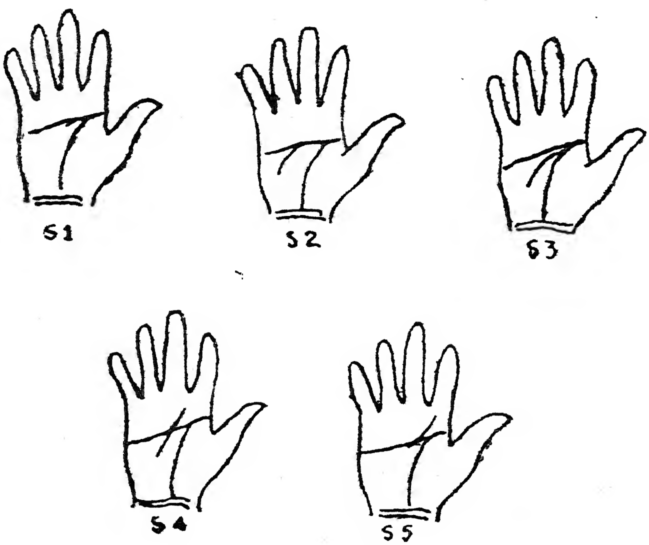

Figure 2

Single Radial Base Crease

accordance with the above definition into further sub-types (Fig. 3, D_1, D_2, D_3, D_4, D_5, D_6). The sub-types of triple radial base crease has not been reported so far (Fig. 4).

The method of crease formulation basis the genetic unity between the various types of creases.

Results and Discussion

To understand certain medical syndromes with the aid of palmar flexion creases the trait appears to be simple and valuable. The existing statistical association makes it possible

for us to speculate about some mechanisms involved in the association between creases and diseases.

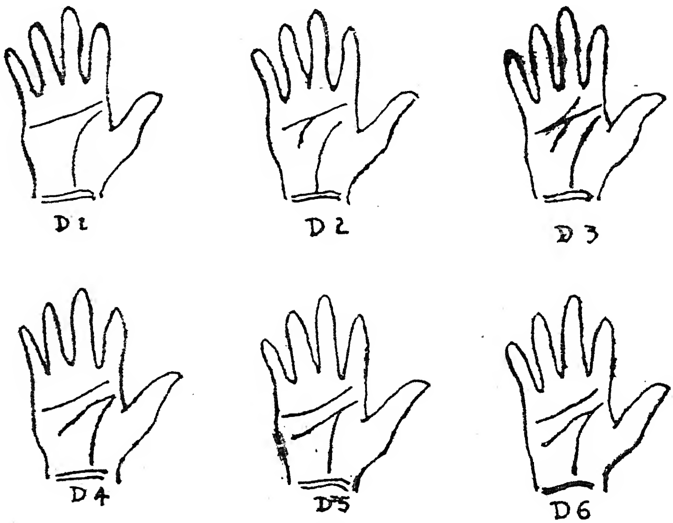

Figure 3

Double Radial Base Crease

A striking association between the creases and Schizophrenia indicate that parallel genetical factors are responsible in the development of the hand and the above disease.

Table 1 represents the three principal types of Palmar flexion creases in patients and in the control group. The frequency of SRBC (29.44%) among the schizophrenic patients is strikingly high as compared to the control group (6.84%). Such high incidence of SRBC has not geen recorded among any

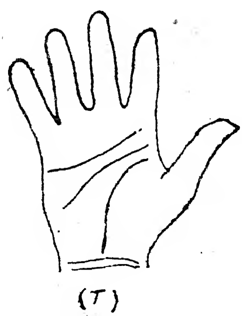

Figure 4
Triple Radial Base Crease

other populations studied so far. The frequency of DRRC also shows marked difference between patients (61.11%) and control group (85.78%), while the frequency of TRBC does not show any marked difference between patients (9.45%) and control group (7.37%).

TABLE 1

Percentage Frequencies of Palmar Creases in Both Hands in Patients and Control Group

Types of Palmar creases	Patients Absolute number	Patients Percentage	Control Group Absolute number	Control Group Percentage
SRBC	53	29.44	13	6.84
DRBC	110	61.11	163	85.78
TRBC	17	9.45	14	7.37
Total	180	100.00	190	100.00

Considering the bimanual distribution of these crease types a strong sinistral dominance of SRBC is noticed (Rt - 26.66% and Lt - 32.23%). While in the control group much difference has not been noticed in right and left palm (Rt - 7.37% and Lt - 6.32%). The frequencies of SRBC and DRBC bear an inverse ratio, while TRBC does not show marked difference (Tables 2 and 3).

TABLE 2

Percentage Frequencies of Palmar Creases in Right Hand in Patients and Control Group

Types of Palmar Creases	Patients Absolute number	Patients Percentage	Control Group Absolute number	Control Group Percentage
SRBC	24	26.66	7	7.37
DRBC	58	64.44	80	84.21
TRBC	8	8.90	8	8.42
Total	90	100.00	95	100.00

TABLE 3

Percentage Frequencies of Palmar Creases in Left Hand in Patients and Control Group

Types of Palmar Creases	Patients		Control Group	
	Absolute number	Percentage	Absolute number	Percentage
SRBC	29	32.23	6	6.32
DRBC	52	57.77	83	87.36
TRBC	9	10.00	6	6.32
Total	90	100.00	95	100.00

Considering the sub-types of the single radial base crease, table 4 exhibits that the frequency of sub-type S_4(12.22%) is strikingly high among the patients as compared to the control group (2.105%). In the same way the presence of sub-type S_1(4.44%) also strikes our mind because it is totally absent in the control group.

TABLE 4

Percentage Frequencies of Sub-Types of Single Radial Base Crease in Both Hands in Patients and Control Group

Sub-types of SRBC	Patients		Control Group	
	Absolute frequency	Percentage	Absolute frequency	Percentage
S_1	8	4.44	0	0
S_2	7	3.89	3	1.58
S_3	12	6.67	5	2.635
S_4	22	12.22	4	2.105
S_5	4	2.22	1	0.552
Total	53	29.44	13	6.845

The bimanual differences of the sub-types of Single Radial Base Crease also shows that the frequency of sub-type S_1 (8.89%) is high on the left hand while it is absent on the right hand. The other sub-types do not show any marked bimanual

differences. In the control group also, no sizable bimanual differences has been observed (Tables 5 and 6).

TABLE 5

Percentile Frequencies of Sub-Types of Single Radial Base Crease in Right Hand in Patients and Control Group

Sub-types of SRBC	Patients Absolute frequency	Patients Percentage	Control Group Absolute frequency	Control Group Percentage
S_1	0	0.00	0	0.00
S_2	4	4.44	1	1.05
S_3	6	6.67	3	3.16
S_4	13	14.44	3	3.16
S_5	1	1.11	0	0.00
Total	24	26.66	7	7.37

TABLE 6

Percentile Frequencies of Sub-Types of Single Radial Base Crease in Left Hand in Patients and Control Group

Sub-types of SRBC	Patients Absolute frequency	Patients Percentage	Control Group Absolute frequency	Control Group Percentage
S_1	8	8.89	0	0.00
S_2	3	3.34	2	2.11
S_3	6	6.67	2	2.11
S_4	9	10.00	1	1.05
S_5	3	3.33	1	1.05
Total	29	32.23	6	6.32

Considering the sub-types of the Double Radial Base Crease (Table 7), it is observed that the frequency of the sub-type D_4 (40%) and D_5 (15.00%) in patients becomes less prominent as compared to the control group (D_4 - 53.15% and D_5 - 28.425%). Tables 8 and 9 does not show any bimanual differences among the sub types of the Double Radial Base Crease neither in the patients nor in the control group.

TABLE 7

Percentile Frequencies of Sub-Types of Double Radial Base Crease in Both Hands in Patients and Control Group

Sub-types of DRBC	Patients		Control Group	
	Absolute frequency	Percentage	Absolute frequency	Percentage
D_1	3	1.67	0	0.00
D_2	1	0.56	1	0.525
D_3	1	0.55	0	0.00
D_4	72	40.00	101	53.15
D_5	27	15.00	54	28.425
D_6	6	3.33	7	3.685
Total	110	61.11	163	85.785

TABLE 8

Percentile Frequencies of Sub-Types of Double Radial Base Crease in Right Hand in Patients and Control Group

Sub-types of DRBC	Patients		Control Group	
	Absolute frequency	Percentage	Absolute frequency	Percentage
D_1	1	1.11	0	0.00
D_2	0	0.00	0	0.00
D_3	0	0.00	0	0.00
D_4	36	40.00	43	45.25
D_5	17	18.88	33	34.74
D_6	4	4.25	4	4.22
Total	58	64.44	80	84.21

TABLE 9

Percentile Frequencies of Sub-Types of Double Radial Base Crease in Left Hand in Patients and Control Group

Sub-types of DRBC	Patients		Control Group	
	Absolute frequency	Percentage	Absolute frequency	Percentage
D_1	2	2.22	0	0.00
D_2	1	1.11	1	1.05
D_3	1	1.11	0	0.00
D_4	36	40.00	58	61.05
D_5	10	11 11	21	22.11
D_6	2	2.22	3	3.15
Total	52	57.77	83	87.36

In tables 10, 11 and 12, the Triple Radial Base Crease does not show any marked difference between the patients and the control group. The Triple Radial Base Crease also fails to indicate any bimanual difference neither in patients nor in the control group.

TABLE 10

Percentile Frequencies of Sub-Types of Triple Radial Base Crease in Both Hands in Patients and Control Group

Sub-types of TRBC	Patients		Control Group	
	Absolute frequency	Percentage	Absolute frequency	Percentage
T_1	17	9.45	14	7.37
Total	17	9.45	14	7.37

TABLE 11

Percentile Frequencies of Sub-Types of Triple Radial Base Crease in Right Hand in Patients and Control Group

Sub-types of TRBC	Patients		Control Group	
	Absolute frequency	Percentage	Absolute frequency	Percentage
T_1	8	8.90	8	8.42
Total	8	8.90	8	8.42

TABLE 12

Percentile Frequencies of Sub-Types of Triple Radial Base Crease in Left Hand in Patients and Control Group

Sub-types of TRBC	Patients		Control Group	
	Absolute frequency	Percentage	Absolute frequency	Percentage
T_1	9	10.00	6	6.32
Total	9	10.00	6	6.32

Association of simian crease with schizophrenia is a well known fact. In the present study association with all palmar creases have been worked out. High frequency of SRBC in

patients and low in the control group shows inverse relationship with the DRBC. Suggestive of the fact that all creases have genetic unity, thus giving the evidence towards the validity of crease formulation which forms the basis of present crease classification.

Considering the sub-types of creases, the sub-types S_1 and S_4 of single radial base crease which predominates the other sub-types in schizophrenic patients. Sub-type S_1 exhibits the sinistral dominance among the schizophrenic patients.

The whole discussion coverages towards a point, that for understanding certain medical syndromes with the aid of palmar flexion creases the trait appears to be simple and valuable. Further this association suggests a parallel development of genetical factors among creases and schizophrenia.

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GENETICS OF QUANTITATIVE CHARACTERS OF HUMAN HEAD HAIR

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Morphological characteristics of human head hair as one of the criteria for racial study has long been recognised. After the re-discovery of Mendelian law attempts have been made to establish the nature of inheritance of different morphological characters of human head hair. It is now well accepted that hereditary factor C is responsible for curvature while the factor S is responsible for spiralization. Both the factors are dominant over smooth and straight forms. Von Verschuer (1927) utilized the morphological characters of head hair as one of the criteria for twin diagnosis and found almost complete concordance in hair characters among the Monozygotic (EZ) twins.

Since the works of Browne (1853) and Pruner-Bey (1883) histological characters of head hair shaft gained its importance in personal identification through the works of Hausman (1934), Keneberg (1935), Wynkoop (1929), Kirk (1940), Steggerda (1940), Seibert and Steggerda (1942), Trotter and Duggins (1950), Shaeuble (1958) and Banerjee (1959–1963). Histological characters of hair shaft such as diameter, medullation, pigmentation, cross-section and weight were studied mainly with respect to age, to hair form and to draw correlation between the above characters to evaluate the nature and significance of the hair shaft characters in personal identification.

It is apparent from the above that hereditary significance of quantitative characters of human head hair shaft has yet to be known. How far the different histological characters of hair shaft are controlled by the genetic component of variability and how far by the non-genetic ones has yet to be thoroughly investigated. With this end in view an attempt has been made to find the role of genetic and the non-genetic component of variability in the manifestation of quantitative characters such as

medullation, hair diameter, cross-sectional index and cross-sectional area and weight of the hair shaft.

MATERIALS AND METHOD

Material for the present study consisted of the hair samples from 48 pairs of German twins comprising the monozygotic (EZ), the same sexed dizygotic (ZZ) and different sexed dizygotic (PZ) twin pairs. All the samples were collected by one of us (A.R.B.) in the Institute of Human Genetics, Muenster, Germany. The zygosity of the twins was established through the similarity method of diagnosis supported by detailed serological tests (ABO, Rh, MNS, P, Kell, Ge, Gm, HP). All the samples were cut close to the scalp following Pinkus (1927). Details of the samples studied for the present purpose have been given in the Tables (1 and 2).

Average age of the male and the female twins included in the present study was 12.1 and 13.9 respectively.

After properly cleaning the samples, 100 strands of hair from each individual were studied for medullation hair diameter (breadth), cross-sectional index, cross-sectional area and weight. Methodology utilized for the study has been described earlier (Banerjee 1965 ; Banerjee and Das-Choudhury, 1969). Thus total number of strands studied in the present investigation was 9600.

For the twin comparison and interpretation of the data mean intrapair variances (Osborne et al 1958 and 1962) of the twin pairs were compared by using 'F' tests. Heretability has been estimated by using Holzinger's formula (1937) in a manner as shown by Neel and Schull (1954); Clark (1956) and Vogel (1961).

Findings on different characteristics of the hair shaft has been given below in the subsequent tables (3 and 4).

TABLE 1

Number of samples according to their sex and zygosity

Twins		Sex			Total
		MM	FF	MF	
Monozygotic		8	9	–	17
Dizygotic	Like sex	17	6	–	23
	Opposite sex	–	–	8	8
Total		25	15	8	48

TABLE 2

Analysis of Variance

Mean intra-pair variances of the different characters of the hair shaft

Characters	Variances						
	Male			Female			
	ME*	EZ	ZZ	ME*	MZ	ZZ	PZ
1. Medullation		.0095	.0716		.0049	.0838	.0279
2. Diameter	.07	9.21	99.28	.16	21.25	132.27	58.84
3. Cross section area	1564.50	26102.93	597020.35	1434.16	26456.37	570775.53	844782.45
4. Weight	.0008	.026	.094	.0006	.063	.167	.293

* M.E. = Mechanical error

TABLE 3

Analysis of Variance – Mean Intra-pair Variances of the Quantitative Characters of the Hair Shaft

Characters	Variances						
	Male				Female		PZ
	ME	EZ	ZZ	ME	ME	ZZ	
1. Medullation		.0095	.0716		.0049	.0838	.0279
2. Diameter	.07	9.21	99.28	.16	21.25	132.27	58.84
3. Index	.0000427	.001203	.0015715	.000041	.00198	.0127	
4. Cross-section area	1564.50	26102.93	59720.25	1434.16	26456.37	570775.53	844782.45
5. Weight	.0008	.026	.094	.0006	.063	.167	.293

TABLE 4

Distribution of F Ratios

	ME male	EZ female	EZ male	ZZ female	EZ EZ male (sex influence)	ZZ ZZ female (sex influence)	EZ male ZZ female (combined)
1. Medulla			7.53	17.10	1.94*	1.17*	10.57
2. Diameter	131.57	132.87	10.77	6.25	2.31	1.34	6.93
3. Index	13.78	19.51	1.21	6.68			2.75
4. Cross-section	16.68	18.44	22.87	21.57	1.01	1.05	22.44
5. Weight	32.87	106.50	3.61	2.65*			2.87

*not significant

TABLE 5

Heritability Estimate

1. Medulla - 90.50%
2. Diameter - 85.57%
3. Index - 63.63%
4. Weight - 65.00%

It will be apparent from the tables (3 and 4) all most all of the variance ratios are statistically significant which is suggestive of the presence of a strong genetic component of variability for the manifestation of the quantitative characters of human head hair. Contribution of sex is found to be very negligible excepting the medullation. It will be further apparent from the table of heritability estimate that a strong hereditary component of variability has been found to be responsible for the incidence of all the quantitative characters of human head hair.

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AN EXPLORATORY STUDY OF MARRIAGE DISTANCE AMONG THE SANTALS IN THE NEIGHBOURHOOD OF GIRIDIH, BIHAR

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INTRODUCTION

One of the vital questions in genetics is "who mates with whom and reproduces how many and what kind(s) of off-spring?" For human populations, where mating is in general governed by the social institution of marriage, the first part of the question may be slightly reformulated as "who marries whom". The question may be asked from very many different standpoints. For instance, "who", "whom" and "what kind(s)" may refer to caste, tribe, religion and such other social group affiliations, to blood groups and such other genetic characters, to anthropometric traits, and so on. In the present study, which considers the first part of the question only, they refer to places of birth of spouses and the linear distance between them.

Marriage distance is an important variable in human genetics, for it determines the extent to which a given gene is expected to move per given unit of time. For various species of Drosophila through studies of dispersion have been made by releasing a known number of marked flies at a given point and recording the number of those recaptured at a given distance after a given period of time (Wallace, 1968). These studies tell us (1) the different probabilities with which individuals move to different distances from their point of origin (release) and the mathematical formulation(s) which describe the relation-ship between the probabilities and distances, and, (2) what the composition of a local population is like, in terms of the spatial distance of the place of origin of its different members,

assuming "emigrants that leave a local population and migrate a certain distance must be replaced in the long run by an equal number of immigrants that have come from the very same distance" (Wallace, 1968) (for without such replacement, certain localities would eventually become too populous and others empty). The studies on Drosophila referred to above consider the physical dispersion of flies as indicator of gene dispersion, for it is assumed that flies moving to a given spot mate and transmit their genes there. In case of humans, physical movements are not necessarily followed by mating, so that a comparable study should refer to physical movement consequent upon marriage rather than physical movement as such.

Population structure has been defined "as the ensemble of known factors governing changes in gene or genotype frequencies other than mutation or selection". It represents the limit set to the action of these two primary evolutionary forces by the fact that any population is not infinite in size, and only approximates the simplifying conditions of random mating, which is the basis of the simplest evolutionary predictions (Cavalli-Sforza, 1958). Population genetics considers two models of population structure (Li, 1955): (1) the *island model* in which "a total population has been subdivided into many isolated groups with a certain proportion of migrants interchanging between them", and, (2) *isolation by distance model* which refers to "a large population which has a continuous distribution over a wide area but in which the mating individuals are restricted to a 'neighbourhood' of a limited distance, so that two remote individuals have practically no chance to mate". These models provide means to measure the degree of differentiation (heterogeneity or variability) within a larger population (Li, 1955).

Model II implies a relationship between the chances of marriage and distance. A population of the second kind is defined in terms of the "neighbourhood" (N). For estimating N we need to estimate the standard deviation of the distance between birth places of parents and offspring. The degree of differentiation, σ^2_q, within a larger population is related to F_r, the inbreeding co-efficient, which in its turn is a function of N

in Model II. Thus, a study of marriage distance helps in (1) defining a population and (2) estimating the degree of differentiation.

Material and Method

In the present study we intend to look at some empirical data with reference to the above-mentioned models. Specifically, we look at the distribution of marriage distance among the Santals in the neighbourhood of the town of Giridih in Bihar. The Santal is an agriculturist tribe numbering over three millions, distributed over a wide area in eastern India. The present data were collected from seven villages located within a radial distance of five miles from Giridih town in the district of Hazaribagh, Bihar. Information was collected from 198 cohorts. Of these, the villages of birth of both the spouses could be located on the map in case of 140 cohorts, which therefor constitute the present sample. The linear distance in miles was recorded for each of these village pairs.

The distribution of marriage frequency by distance has been given in figure 1. The distances were grouped in intervals of three miles, and the mid-points of these distances were written as 1, 2, ..., 9, for the purpose of this analysis. A Type III Pearsonian curve of the equation

$$y = 42.640(1 + x/2.021890)^{2.544274} e^{-1.258364 x},$$

where y = height of the ordinate, $x = x^1 -$ mode (the curve has origin at mode) x^1 = (actual distance + 1.55)/3 miles, was fitted to the observed distribution of marriage frequency by distance. The method described by Elderton (1953) was followed in fitting the curve. Chi-square test showed that the fit between the observed and the expected frequencies was good (chi-squre = 5.086, d. f. 3, $.20 > P > .10$). The distribution shows that the highest frequency occurs at a moderate distance – the third distance class in case of the observed and the second one in case of the expected – but not at distance zero (i. e., the same village). The mean marriage distance was 6.742 miles with a standard deviation of 4.571 miles.

Discussion

In what follows, we have proposed some possible explanations for such a distribution. Later, we have compared this

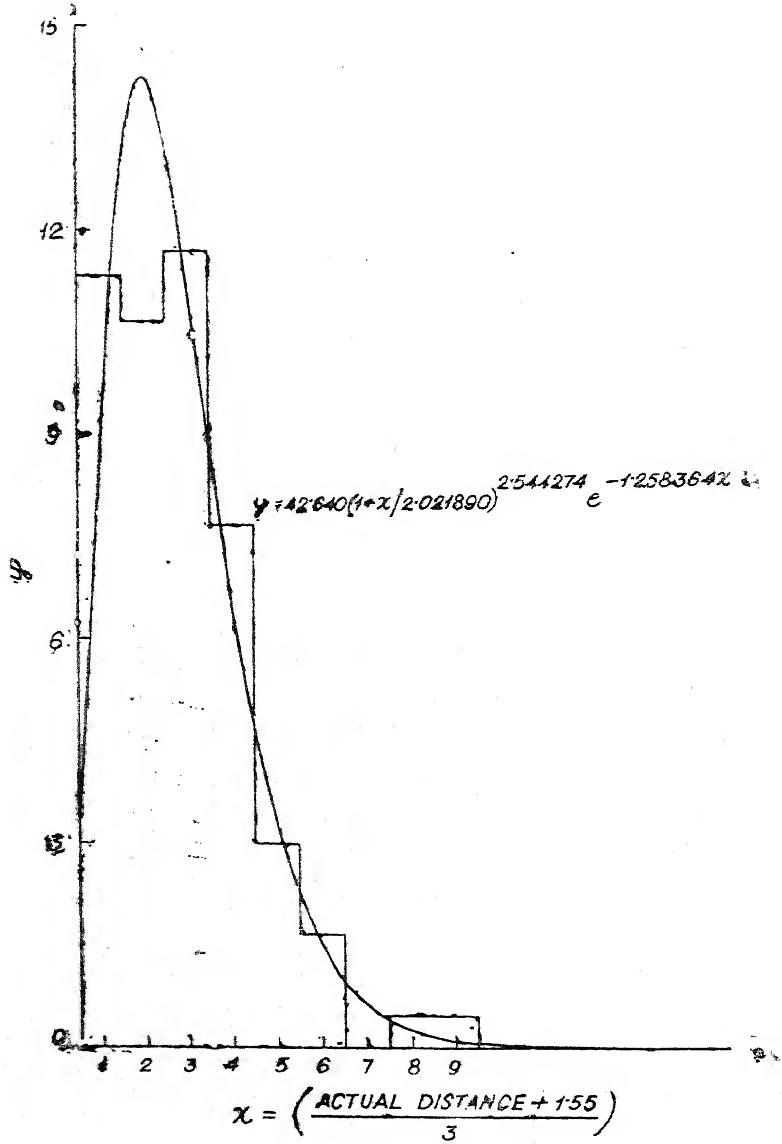

Figure 1

Distribution of Marriage Frequency by Distance

distribution with those obtained elsewhere and, again, proposed some possible explanation for the difference between them. The proposed explanations are all tentative in nature and are subject to verification.

The probability of marriage seems to be determined by many factors:

(1) In general, marriages are not contracted between total strangers. An individual would tend to marry into an area and a family he has some knowledge of. Given the limited transport and communication facilities available to the tribals, who thus have to walk to most of the places they want to visit, the amount of an individual's knowledge of another village is expected to depend considerably on the distance of the second village from his own. And, if the amount of neighbourhood knowledge decreases with increasing distance, the chances of marriage will correspondingly decrease in the same direction, the chances being the highest at one's own village for which neighbourhood knowledge is maximal. This explanation seems to fit in with the distribution from the third distance class onwards, but apparently does not do so with the initial part of the curve where the frequencies decrease towards shorter distances rather than increasing.

(2) Availability of mates is likely to be an important factor. Availability at a certain village would tend to depend on the size of this village. If all the villages considered in a certain study were of the same size at least as far as the marriageable age group is concerned, village size would not need to be taken into consideration. But if with reference to a particular village the sizes of the surrounding villages were distributed such that those within the range of the second distance class were the largest, the size decreasing gradually to both longer and shorter distances, we could have obtained a distribution like the one we have actually obtained. However, such a distribution of the size of the surrounding villages, even with reference to the seven villages we have data from, is unlikely. An adjustment for differential village size could be made by dividing the observed frequency of marriage between two villages by the product of the two village sizes, summing the quotients for all village pairs at the same distance and using these sums as

the observed y values. Such an adjustment was not attempted in the present analysis but it could be done.

(3) Availability of mates at a certain village does not depend only on the number of individuals of the marriageable age group in that village. An individual may have a large number of persons of the marriageable age and the opposite sex in his own village, but, given the patrilocal society like the Santal's and given the rules of sub-clan exogamy, a large proportion of them will be related to him through the male line of descent, will be of his own sub-clan and therefore prohibited mates, Given a patrilocal society, one can presume that an individual's relatives through the male line of descent will be concentrated in his own village and the ones nearby, the proportion of such relatives to the total population of a village decreasing to villages farther and farther away, eventually to reach a limiting point after which there will be practically no change in the proportion. Probably, we are dealing here with two factors, the combined effect of which gives the observed distribution : (1) neighbourhood knowledge which is the highest for one's own village of origin and decreases gradually with increasing distance, and, (2) proportion (number of available mates at a given village) / (total population in this village) which is the lowest in one's own village (since the proportion of prohibited mates is the highest at one's own village) and increases rapidly with distance to reach a limiting point. It would be interesting to evaluate these two factors separately, formulate the relationship of each with distance and to check if their distributions conform with our hypothesized patterns. Further, one could test if an analysis taking into account both the factors simultaneously will give us the distribution shown in figure 1. In order to do this we have to find some method for quantifying neighbourhood knowledge.

(4) The amount of neighbourhood knowledge one posses-ses is decidedly determined by various factors. For instance, if a large industrial enterprise develops at a certain place, rural people from a wide area around this place would move into this place in search of jobs. If they were able to secure jobs here, as many of them certainly would, they would spend large parts of their time at this place, would eventually become familiar with

other people moving in here and also with the immediate neighbourhood of this place. In a situation like this, the amount of knowledge an individual is likely to have about another village could not be defined merely as a function of distance. Consequently, the probability of marriage could not be defined in terms of distance either, in such a situation. Further, the total socio-economic environment at the industrial set-up, being so very different from the tradition-oriented environment an individual was born and grew up in, might lead to a drastic change of the values and norms, which in its turn might affect the marriage patterns among many other components of the social life. It would be interesting to study the populations working in one of the industrial complexes in India. It would also be interesting to study the Santal, Oraon, Munda, etc., tea garden labourers in Assam who migrated to their present habitat from the Chotanagpur area. The bulk of the migration occurred probably a couple of generations ago, so that the initial period of uncertainity in a unfamiliar environment is over, new, changed values and norms have emerged and new patterns of marriage, if any, have tended to stabilize. Does the relationship between marriage frequency and marriage distance, as found in our sample, exist among the migrants? Do they still stick faithfully to the traditional rule of tribal endogamy, even if in order to find a mate from one's own tribe one has to cover a considerable distance? Do groups of the same tribe immigrating to the tea gardens from widely separated source areas consider themselves members of the same mating group or do they maintain their original regional distinctions even in the new habitat so as to form a series of exclusive entities? These are some of the questions which may profitably be asked in order that the pattern of gene dispersion in India may be understood as a dynamic process set in the perspective of an ever-changing socio-economic context. A comparative study of rural and urban populations between which the values may widely differ may also be worthwhile.

5. Marriage within the same village may be considered undesireable, for, if it does occur, there will be chances of the delicate details about the happenings in one's family to be communicated to another, i.e., by the wife to her paternal home, which will be an unwanted encroachment on the privacy of the

former on the one hand, and on the other, may provoke the wife's kins to interfere in the affairs of the former, at least in the interest of their daughter, so that eventually strained relationship, tension and quarrel might follow. This possibility could be avoided by marrying into a village located at a reasonable distance, so that the wife would not be able to run home every now and again. Even if she does so once in a while, her kins would not be able to visit the husband's home often and interfere. The restricting effect of this factor is expected to be limited to a certain distance. Given (1) this reluctance to intra-village marriage and (2) the relationship between spatial distance and neighbourhood knowledge, and neighbourhood knowledge and probability of marrirge, there should be an optimal distance around which most of the marriages will be contracted and away from which the frequency will gradually fall. Again, one should perform an analysis taking into account all the factors simultaneously. To do so, one would have to find a method to quantify: "reluctance". Among the Santals Culshaw (1949) states that there actually is such a reluctance, for it is believed that for the husband's family it would be difficult "taming" a girl whose parents stay so near that she can run back to them often enough.

In stating the above-mentioned explanations we are not by any chance ruling out the possibility of still others, which may be operative in general or in specific populations, all of which should be carefully recorded and analysed in a comprehensive study of marriage distance.

Comparing the distribution obtained in the present sample with that obtained by Cavalli-Sforza (1958) we find that while in our data the curve rises from distance zero to a peak and then gradually falls off, in the latter sample, it has its highest point at distance zero. A curve of the type $F=e^{-k\sqrt{r}}$ (r=distance) was, with suitable adjustment for differential village size, gave a good fit to the Parma data. Similar types of curves, $f=ae^{-bd}$ and $f=dae^{-b\sqrt{d}}$ (d=distance), were fitted to Sutter and Tran-Ngoc-Toan's (1957) French data and Fraccaro's (1959) Swedish data ($f=ae^{-bd^{1/5}}$, where d=distance). The Oxfordshire data of

Boyce *et al* (1966–67) is presented in a somewhat different form, but when plotted in the form we have adopted, give a distribution more like ours than like those of Cavalli-Sforza (1958), Sutter and Tran-Ngoc-Toan (1957) and Fraccaro (1959). Schull and Neel (1965) also state that in their Japanese sample the frequency increases to an optimal point from distance zero and then falls off again.

Again, we may speculate on the possible explanation of the similarities and differences among the several samples described above:

(1) Whereas among the Santals the chances of marriage within one's own village or to those too closeby is low for reasons that (a) there is a social reluctance to intra-village marriage and (b) availability of mates in one's own village is low, for many of the individuals in it are related to one through the male line of descent and therefore are prohibited mates, these factors may not be operative in Parma – indeed, parallel first cousin marriage occurs there although they are considered undesirable – so that spatial distance may be the most dominant factor determining marriage frequency. Whether the same explanation holds for the French and the Swedish data cited above we do not know. Nor can we guess whether the explanations proposed for the low intra-village marriage frequency among the Santals hold for the Oxfordshire and the Japanese data. However, Schull and Neel (1965) suggest, as a possible explanation of the distribution obtained by them, some kind of restriction on intra-village marriage due to the rules of exogamy, etc., operating in Japan.

Admittedly, this paper raises many more questions than it has been able to answer. It does so deliberately. However, we have tried only to look at some data from the standpoint of generating hypotheses rather than testing them.

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DYNAMICS OF ABO GENE FREQUENCY VARIATIONS IN TIBET

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INTRODUCTION

Reports on blood group distribution in Tibetans have appeared in the past from time to time (Macfarlane '41, Buchi '52, Prince Peter '61). More recently blood group picture of Tibetans has been extended to include observations on ABH Secretion (Bhalla and Kaul '66 and Tiwari '66) and Rh, MNS and Kell Systems (Tiwari '66). However, the state of our knowledge with regards to variations in the incidence of blood groups in Tibet, has not advanced beyond a generalised account of blood group distribution in Tibetans taken as a whole. Ethnically the Tibetans constitute a heterogeneous stock of people. It is, therefore, not unlikely, if a differential fixation of allele frequencies is revealed within the Tibetan racial complex. It must be reckoned that geographical barriers in Tibet have been fairly effective in restricting the movements of people and thus the gene flow to relatively narrower confines, splitting the population into reproductive isolates. Geographically, three regions can be demarcated as primary centres of Tibetan concentration namely Kham (eastern Tibet), U-Tsang (Central Tibet), and Nga-Ri (Western Tibet). Locked up into these geographical recesses, till recently; Tibetans remained virtually cut off from rest of the world by the intervening mass of high mountains, movements across which could be possible only through difficult passes. They bred in relative isolation for centuries together. Their contact with the outsiders was scant and noticeable to any appreciable extent only in the peripheral areas. While in the eastern parts, Tibetans have a long history of contact with the Chinese of Szechuan and Yunnan and nomad Mongols bearing allegiance to Chinghai,

those in Central Tibet have lived in relative seclusion. In contrast to central and eastern Tibet, the highlands of western Tibet are sparsely populated. Here too the Tibetans have had a long span of contact with the native populations of India in the border districts of Garhwal, Kinnaur, Kulu, Lahul-Spiti and Ladakh, rendering a composite character to people in these districts as a result of intermixture.

Material and Method

Three groups of Tibetans have been delineated on the basis of their place of origin in Tibet, viz. central Tibetans, eastern Tibetans and western Tibetans and the data processed accordingly, with a view to ascertain variations in allele frequencies within the Tibetan racial complex. Blood samples of 182 individuals (100 central Tibetans, and 42 Eastern Tibetans and 40 Western Tibetans) were examined following the usual open slide technique. The subjects were selected at random from amongst the Tibetan immigrants at Dharmasala (H.P., India), where the Tibetan refugees have settled in large number sequel to political changes of 1959 in Tibet.

Discussion

The results of blood group investigation in Tibetans are shown in Table 1. The blood group distribution in Tibet is characterised by and exceedingly high incidence of group-O in central Tibetans, a rise in the incidence of both A and B at the expense of O in Eastern Tibetans and an excess of B at the expense of both A and O in Western Tibetans. Viewing the distribution in terms of gene frequencies, it is seen that gene 'r' is most concentrated in the central Tibet (.688) and its frequency shades off towards peripheral areas in the east (.582) and the west (.607). Although, the homogeneity test does not reveal statistically significant differences at 5% level in the incidence of blood groups in three groups of Tibetans, none the less, the ABO gene frequency distribution in Tibetans does help in the construction of genoclines that reveal the trend of variation on the plateau. There is an unmistakable rise in B, associated with a decline in the incidence of O as we move away from central Tibet towards east and west. As against this, the distribution of A is inconsistent and the variations are less marked than in B and O.

TABLE 1

Population	No.	O	A	B	AB	p	q	r	X^2	Probaility for 2. d. f.
Tibetans (Central)	100	44 (46.0)	19 (19.0)	28 (28.0)	7 (7.0)	.129	.183	.688	1.18	.70>P>.50
Tibetans (Eastern)	42	14 (33.33)	9 (21.43)	15 (35.71)	4 (9.52)	.163	.255	.582	0.08	.99>P>.90
Tibetans (Western)	40	14 (35.00)	6 (15.00)	16 (40.00)	4 (10.0)	.1164	.277	.607	.81	.70>P>.50
Tibetans (Combined)	182	74 (40.66)	34 (18.68)	59 (32.42)	15 (8.24)	.136	.218	.646	1.80	.50>P>.30

TABLE 2

Population	X^2	Probability for 3 d. f.
C.T.×E.T.	3.257	.50>P>.30
C.T.×W.T.	2.70	.50>P>.30
E.T.×W.T.	0.586	.90>P>.70

The exact picture of blood group variations in Tibetans need to be examined in the light of contacts which Tibetans have had in the past. Undoubtedly the geography of Tibet has been a primary factor not only in restricting the movements of people to relatively narrower confines, but also in exposing the Tibetans living in the east and west to outside influence more than the central Tibetans. Historical records show that, while the Tibetans in the east have had a long period of contact with the Chinese of Szechuan and Yunan provinces, those in the west, similarly, have had a long span of contact with the Cis-Himalayan populations along the northern border of India. In genetic terms, however, the effect of these contacts appears to have been more pronounced in the Eastern Tibet and reasonobly so, because this region has been a centre of vigorous human activity unlike the desolate and sparsely populated region of Nga-Ri (Western Tibet). Kham is more populous than other parts of Tibet and owing to heavier rainfall, also more fertile and agriculturally better developed. It is marked with important trade routes to Szechuan across Sikang, to Yunan between upper courses of Mekang and Salween, to Shinghai via Jye-Kun-Do and Lhasa through Kang-po, which facilitated easy movement of, and greater contact with foreign elements.

The blood group allele frequencies in the Eastern and Western Tibetans, as reported here, do reflect cross-currents of gene flow with neighbouring populations at the two ends. The contention that the Tibetans in the east and west have been in genetic communication with the neighbouring populations in Western China and Northern India is further strengthened when the blood group picture of populations in the vicinity of Tibet is examined (Table 3). The p, q, r frequencies reported in these populations by different authors are plotted on a three co-ordinate graph (Fig. 1). It is seen that the central Tibetans fall in the zone of High O, and come close to some of the populations in China (Canton and Szechuan) in this respect. They are bound by Western Tibetans on one side, who fall in the belt of high B along with some other populations mainly of Indian origin, namely, Rajputs (Rampur Bushahr), Punjabi Hindus, Kumaoni Rajputs etc. on the other

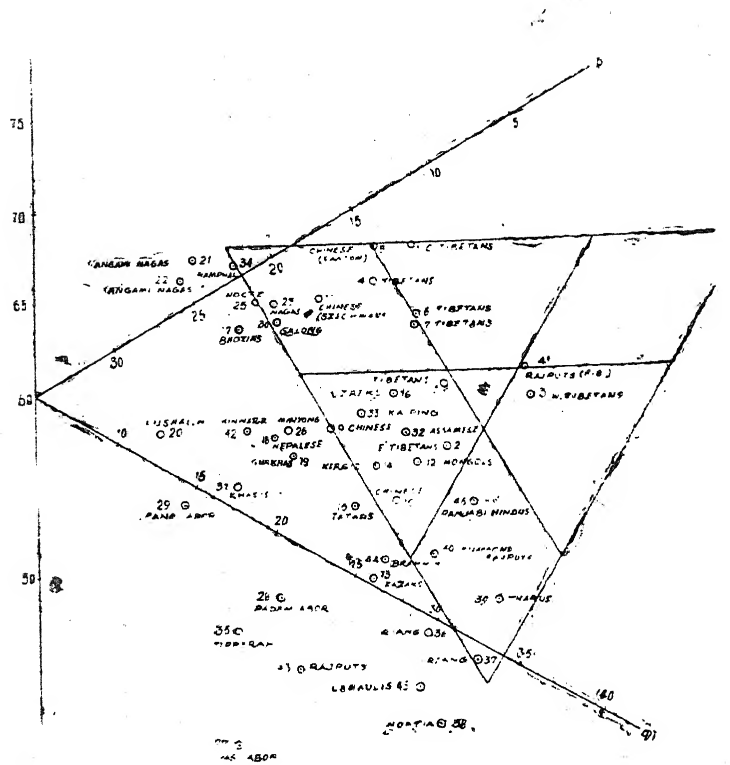

Figure 1
Three Co-ordinate Graph

side are the eastern Tibetans who fall in the belt of relatively high A with moderate to high incidence of O, and form a cluster along with populations like Uzobecks, Kaiping, Assamese, Mongols, Kirghis, Tatars, Chinese etc. It can be made out from the pattern of distribution as seen on the three co-ordinate graph that, while the central Tibetans, confined to their geographical environs and out of easy reach from all sides, retained a high incidence of group O, those in the east as well as in the west were open to the exchange of genes at either ends. Two main genetic strains can be earmarked; one composed of the Mongoloid Complex influencing the genetic composition of Eastern Tibetans, and the second a Mediterranean Complex spanning the northern frontiers of India and

TABLE 3

S. No.	Population	Place	No. tested	O	A	B	AB	p	q	r	Investigator
1.	Tibetans (Central)	Refugees in India	100	46.00	19.00	28.00	7.00	.129	.183	.688	Present study
2.	Tibetans (Eastern)	-do-	42	33.33	21.43	35.71	9.52	.163	.255	.582	-do-
3.	Tibetans (Western)	-do-	40	35.00	15.00	40.00	10.00	.116	.277	.607	-do-
3-a.	Tibetans (Combined)	-do-	182	40.66	18.68	32.42	8.24	.136	.218	.646	-do-
4.	Tibetans	Rahla	62	41.93	22.58	25.81	9.68	.157	.178	.665	Bhalla & Kaul, 1968
5.	Tibetans	—	284	—	—	—	—	.154	.242	.600	Prince Peter *et al*, 61
6.	Tibetans	—	—	—	—	—	—	.147	.212	.614	Buchi, 1952
7.	Tibetans	Refugees	290	40.69	21.38	32.07	5.85	.1500	.2127	.6373	Tiwari, 1966
8.	Chinese	Canton	992	45.9	22.8	25.2	6.1	.152	.166	.676	Dormanns (c. f. Hooton)
9.	Chinese	Hoang Ho	2127	34.2	30.8	27.7	7.3	.220	.201	.587	Yang-Fung-Min (-do-)
10.	Chinese	Peking	1296	28.6	26.6	32.0	12.8	.208	.244	.535	Huie (-do-)
11.	Chinese	Szechwan	1000	44.8	28.9	23.7	2.6	.188	.157	.655	Lo & Yang (c.f. Gates)
12.	Mongols	Urga	114	28.6	23.2	31.3	16.9	.185	.239	.535	Jettwar (c. f. Hooton)
13.	Kazaks	Ksylorda	1172	23.7	29.3	31.5	15.5	.241	.256	.497	Grubina (-do-)
14.	Kirgiz	Army	500	31.6	27.4	32.2	8.8	.2061	.236	.563	Askmazin (-do-)
15.	Tatars	Kazan	500	27.8	30.0	28.8	13.4	.233	.225	.527	Schwartz Nintsovitskaya (c. f. Hooton)
16.	Uzbeks	—	153	36.6	24.8	32.0	6.6	.178	.223	.599	Wellisch, 1935 (c. f. Gates)
17.	Bhotias (born in C. Tibet)	Tibet	80	38.75	36.25	20.00	5.00	.234	.134	.622	Macfarlane, 1941
18.	Nepalese	Kalimpong	78	33.30	34.60	23.10	9.00	.249	.176	.577	Macfarlane, 1937
19.	Gurkhas	Nepal	2869	31.8	33.8	25.2	9.2	.245	.190	.565	Agar, 1946

20.	Lushai Nagas	—	141	37.62	44.68	16.31	6.38	.3016	.1213	.5771	Mitra, 1936
21.	Angami Nagas	Burma Border	165	46.06	38.79	11.51	3.64	.2413	.089	.6798	– do –
22.	Angami Nagas	Naga Hills	100	45.00	38.00	11.00	6.00	.2503	.085	.6692	Bhattacharjee, 1957
23.	Angami, Lahotas, Rengmas, Sema Naga	– do –	140	40.00	33.57	22.14	4.29	.2131	.1433	.6436	Br. Assoc. Res. Com. 1939
24.	Konyaks	– do –	127	45.67	40.16	10.24	3.94	.250	.071	.678	– do –
25.	Nocte	NEFA	313	41.22	31.14	20.13	3.51	.484	.1271	.6545	Bhattacharjee, 1954
26.	Minyong Abor	Abor Hills	553	35.08	32.55	22.42	9.95	.2403	.1766	.5831	– do –
27.	Pasi Abor	– do –	191	19.4	37.7	22.5	20.4	.3463	.2400	.4134	– do –
28.	Padam Abor	– do –	754	24.27	36.07	26.0	13.66	.2900	.2224	.4875	– do –
29.	Pangi Abor	– do –	197	27.41	45.69	20.30	6.6	.3127	.1466	.5407	– do –
30.	Galong Abor	– do –	400	40.75	32.25	20.75	6.25	.216	.145	.639	Kumar, 1954
31.	Khasis	Cherapunji	200	33.00	35.00	18.50	13.50	.2779	.1726	.5495	Macfarlane, 1941
32.	Assamese	Dibrugarh & other areas	2000	33.65	24.55	32.55	9.25	.186	.237	.580	Mitra, 1933
33.	Kaiping	Tripura	100	38.00	24.00	26.00	12.00	.1971	.2095	.5934	Gupta, 1958
34.	Ramphal	– do –	100	46.00	33.00	15.00	6.00	.2181	.1107	.6712	– do –
35.	Tipperah	– do –	150	21.33	41.33	25.33	12.00	.3190	.2097	.4713	– do –
36.	Riang	– do –	150	22.00	27.33	37.33	13.33	.2301	.2981	.4718	– do –
37.	Riang	– do –	509	19.84	25.15	42.04	12.97	.2147	.3312	.4541	Kumar & Sastri, 1961
38.	Noatia	– do –	142	16.20	28.87	40.84	14.08	.2477	.3327	.4196	Kumar, 1960
39.	Tharus	– do –	240	27.08	17.08	37.50	18.33	.1913	.3267	.4820	Mujumdar, 1943
40.	Kumaoni Rajputs	Almora	124	29.03	24.19	33.87	12.90	.2052	.2682	.5266	Tiwari, 1954
41.	Rajputs	Rampur Bushahr	126	29.36	13.49	37.30	19.84	.113	.275	.541	Punjab Univ., 1962
42.	Kinnar Kanets	Chini Valley	310	32.90	37.42	22.26	7.42	.258	.162	.579	Bhalla, 1961
43.	Rajputs	Kulu & Katrain	268	21.64	34.7	27.61	16.04	.2983	.2494	.4651	Delhi Univ., 1958
44.	Brahmins	Chamba	147	24.49	30.61	35.37	9.52	.229	.260	.519	– do – 1959
45.	Lahaulis	Lahaul	306	17.00	31.20	39.50	11.70	.250	.310	.439	Chopra & Sidhu, 1970
46.	Punjabi Hindus	Delhi	1284	28.65	22.67	39.72	8.96	.1741	.2863	.5396	Bhalla, 1963

influencing the genetic makeup of Western Tibetans. While the former appears to have been more effective in inducing the process of genetic assimilation, in comparison to the latter, the proper assessment of its magnitude at the two ends can be made out only after more detailed studies are carried out along these lines.

Summary

Three groups of Tibetans have been delineated on the basis of their place of origin in Tibet viz. Central Tibetans, Eastern Tibetans and Western Tibetans and the blood group data processed accordingly with a view to ascertain variations in allele frequencies within the Tibetan racial complex. The results of the study reveal some interesting trends of gene frequency variation in Tibet. An exceedingly high incidence of gene 'r' is recorded in Central Tibetans which shades off towards peripheral areas of Tibet in the east and west. The variations observed in the distribution of ABO blood groups in Tibetans are discussed in the light of blood group picture obtaining in the neighbouring populations and the factors contributing to the dynamics of gene flow in Tibet are earmarked.

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CHROMOSOMAL ABERRATIONS IN CHILDREN BORN OF CONSANGUINEOUS MARRIAGES

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INTRODUCTION

Genetic disadvantages of consanguineous marriages are generally agreed upon, but their precise nature still remains to be specified. Likewise the genesis of trisomic aberrations is mostly a matter of surmises. Scientific studies are now being directed towards the investigation of the predisposing factors that may favour the occurrence of nondysjunction in the maternal germ plasm, in such cases.

Based on an analogy with Drosophila, Penrose (1961) has postulated that man might harbour recessive genes, which are apt to cause nondysjunction of 21 chromosome in ova of homozygous females. This hypothesis is suggestive of a higher frequency of consanguinity in maternal grand parents of children having trisomy 21. Simultaneous occurrence of Down's and Klinefelter's syndromes may be a further evidence of a tendency of one parent towards nondysjunction.

In the social set up of Pondicherry, consanguineous marriages, especially of the maternal uncle-niece type, are frequent. In some families such marriages have taken place for successive generations. Thus, Pondicherry provides a unique opportunity for a testing of the above hypothesis.

The present paper is an attempt towards an investigation of a relationship, if any, between consanguineous marriages and chromosomal aberrations.

MATERIAL AND METHODS

The present series includes a study of clinical and cytogenetic features of 44 cases with chromosomal aberrations.

The bone marrow aspirates were used for preparing karyotypes by a modified version of Hungerford's method (1965), reported earlier (Bhargava et al, 1971). Relevant genealogical information regarding the consanguineous marriages, was obtained from reliable sources in the family.

Observations

In the present study, trisomy 21 is the most frequent chromosomal aberration – 33 cases, followed by trisomy D – 6 cases; Trisomy E – 2 cases; one case each of Trisomy 22, Cri du chat and Turner's syndrome.

The relative incidences of consanguineous marriages in these cases is presented in Table 1.

31 cases out of 44 were born of consanguineous marriages.

Table 1

Showing Incidence of Consanguinity and Chromosomal Aberrations

Chromosomal aberrations	Consanguinity Present	Consanguinity Absent	Total
Trisomy 21	22	11	33
Trisomy D	5	1	6
Trisomy E	2	–	2
Trisomy 22	1	–	1
Cri du chat syndrome	1	–	1
Turner syndrome	-	1	1
Total	31	13	44

The maternal uncle-niece type of marriage either as such, or in succession to similar marriages in previous generations, is seen more frequently than the first cousin type.

TABLE 2

Showing Relationship of Cromosomal Aberrations and Type of Consanguinity

Chromosomal aberrations	Type of consanguinity Uncle-niece	First cousin	Combined	Total
Trisomy 21	6	4	12	22
Trisomy D	2	3	–	5
Trisomy E	1	–	1	2
Trisomy 22	1	–	–	1
Cri du chat syndrome	1	–	–	1
Total	11	7	13	31

The specific nature of the chromosomal aberration seems to be independent of the parity of the mother (Table 3) and number of generations of consanguinity (Table 4).

TABLE 3

Showing Inter-Relationship of Chromosomal Aberrations, Parity and Consanguinity

Chromosomal aberrations	Parity 1 C+Ve	1 C–Ve	2 C+Ve	2 C–Ve	3 C+Ve	3 C–Ve	4 C+Ve	4 C–Ve	Total
Trisomy 21	6	1	3	6	2	1	11	3	33
Trisomy D	–	–	2	1	1	–	2	–	6
Trisomy E	–	–	1	–	–	–	1	–	2
Trisomy 22	1	–	–	–	–	–	–	–	1
Cri du chat syndrome	–	–	–	–	1	–	–	–	1
Turner syndrome	–	–	–	–	–	1	–	–	1
Total	7	1	6	7	4	2	14	3	44

C denotes consanguinity

TABLE 4

Showing Relative Incidence of Chromosomal Aberrations and Generations of Consanguinity

Chrmosomal aberrations	Generations of Consanguinity 1	2	3	4	Total
Trisomy 21	7	7	7	1	22
Trisomy 22	1	–	–	–	1
Trisomy D	2	2	–	1	5
Trisomy E	–	2	–	–	2
Cri du chat	–	1	–	–	1
Total	10	12	7	1	31

The incidence of chromosomal aberrations as such, appears to be more frequent with the maternal uncle-niece type of marriage and younger maternal age (Table 5), with a mean maternal age (i.e. 27.93±5.6 years).

TABLE 6

Showing Inter-Relationship of Chromosomal Aberrations, Maternal Age and Consanguinity

Chromosomal aberrations	Age of mother 20–25 yrs. C+Ve	C–Ve	26–30 yrs. C+Ve	C–Ve	31–35 yrs. C+Ve	C–Ve	Above 35 yrs. C+Ve	C–Ve	Total
Trisomy 21	7	4	5	3	5	3	5	1	33
Trisomy D	2	1	3	–	–	–	–	–	6
Trisomy E	–	–	2	–	–	–	–	–	2
Trisomy 22	1	–	–	–	–	–	–	–	1
Cri du chat syndrome	–	–	1	–	–	–	–	–	1
Turner syndrome	–	–	–	–	–	1	–	–	1
Total	10	5	11	3	5	4	5	1	44

C denotes consanguinity

The effects of consanguineous marriages in relation to the above, do not show any exaggeration with more generations of consanguinity (Table 7)

TABLE 7

Showing Relationship of Generations of Consanguinity and Maternal Age

Generations of consanguinity	Age of mother 20–25 yrs.	26–30 yrs.	31–35 yrs.	above 35 yrs.	Total
One	5	3	1	1	10
Two	2	5	2	3	12
Three	2	2	2	1	7
Four	1	1	–	–	2
Total	10	11	5	5	31

The analysis of the maternal age and the type of consanguineous marriage is suggestive of a relationship between younger maternal age and the maternal uncle-niece marriage.

TABLE 8

Showing Relationship of Type of Marriage and Maternal Age

Type of marriage	Maternal age 20–25 yrs.	26–30 yrs.	31–35 yrs.	above 35 yrs.	Total
Maternal uncle-niece	5	4	1	1	11
First cousin	3	3	1	–	7
Combined	2	4	3	4	13
Total	10	11	5	5	31

The salient features of the phenotype, though plemorphic, do not show any specific modifications in severity of their manifestations, in cases with consanguineous marriages.

Cytogenetically, mosaicism was found in only two cases – a case of trisomy 22 which showed mosaicism with monosomy 22 trisomy 22 with and without G/G translocation and another, a Turner's syndrome, XY/XO Mosaic. All the cases except Cri du chat syndrome, showed a trisomic karyotype. Translocations were not seen in any of these cases. A chromosomal discordance of 21 chromosome was observed in a pair of

monozygotic twins – heterokaryotic monozygotism, diplo 21 – triplo 21 variety. These twins had an ineffective mosaicism, consequent to an arterial anastomosis between two components of the placenta.

Discussion

It can be surmised that in absence of cytogenetic abnormalities like trisomy or translocations in mothers of a younger age, the primary nondysjunction is facilitated by maternal genetic factors, or by unidentified environmental influences like toxins, radiations, viruses or possibly a consanguineous marriage (Balakrishnan et al, 1970).

The present series has a very high incidence of trisomic syndromes in children born of relatively young mothers (Mean maternal age 27.93 ± 5.6 yrs.), after a consanguineous marriage, mostly of the maternal uncle-niece type, for a number of generations. In addition to above, the variegated nature of chromosomal aberrations and absence of translocations, in the present study, apparently lend considerable support to Penrose's hypothesis (1961), of recessive genes causing nondysjunction in ova of homozygous females.

These inferences are not in agreement with most of the earlier reports based on a smaller number of consanguineous marriages, only of the first cousin type, like in Sweden (Forssman, 1967) Japan (Matsunaga, 1967) and Britain (Berg, 1967).

This discordance can largely be accounted for by a larger number of cases, and consanguineous marriages of the maternal uncle-niece type over successive generations, being included in the present study. It is likely that such marriages, facilitate the operation of recessive genes of the maternal side. However, the possibility of the tendency for nondysjunction, being exaggerated as such in young mothers after consanguineous marriages, and the nonspecific nature of chromosomal aberrations in consanguinity, being suggestive of a dominant gene action cannot be ruled out.

The present findings are only suggestive of a relationship between chromosomal aberrations and consanguineous marriages. A further elucidation of these suggestions by studies

on a larger number of such cases, as a survey of consanguineous marriages and congenital malformations, in conjunction with karyotypes, is contemplated.

Summary

Although random references to genetic drawbacks of consanguineous marriages have been made, yet their relationship with chromosomal aberrations has not been confirmed. The high incidence of consanguineous marriages in Pondicherry, provide a unique opportunity of testing Penrose's hypothesis (1961) of recessive genes causing nondysjunction in ova of homozygous females.

In a clinical, cytogenetic and pedigree study of 44 cases of chromosomal aberrations (including Trisomy 21 – 33 cases; Trisomy D – 6 cases; Trisomy E – 2 cases; Trisomy 22 – 1 case) a history of consanguineous marriage – (maternal uncle-niece or first cousin type), for 1 to 4 generations was found in 31 cases.

The data in relation to type of chromosomal aberration, maternal age and parity, the type of consanguineous marriage and the generations involved, have been analysed. The type of aberration, seems to be independent of parity and generations of consanguinity. The findings suggest that incidence of chromosomal aberration has a rather nonspecific relationship with younger maternal age, and maternal uncle-niece type of marriage. More generations of consanguineous marriages do not seem to modify this relationship.

Cytogenetically none of the Trisomy 21, or Trisomy D cases showed a translocation. The phenotype did not show any significant modifications with consanguinity.

The high frequency of trisomic syndromes in children born of young mothers, married to their maternal uncles, apparently lends support to Penrose's hypothesis, and disagrees with other reports from Sweeden (Forssmann, 1967), Japan (Matsunaga, 1967) and U. K. (Berg, 1967).

Significance of these observations and the avenues of further studies, proposed on a larger number of cases, are discussed.

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A STUDY OF SOME GENETICAL MARKERS AMONG THE TWO TRIBES OF COASTAL ANDHRA PRADESH

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INTRODUCTION

A population genetical study of the two major tribes, Konda Reddi (K. R.) and Koya Dora (K. D.) in Rampachodavaram Block (agency area of East Godavari District, Andhra Pradesh, India), was undertaken during October-November, 1970 with a pilot survey of the area in September, 1970.

The area of the block is about 190 square miles with a population of 25,151 individuals, where a total of 16,387 tribal populations have been recorded (according to the Census of 1961). There are five major tribal groups in this area, but predominantly inhabited by the Konda Reddi and Koya Dora tribes. Rampachodavaram Block villages are isolated from one another and all the tribes are mainly agriculturalists. They speak Telugu and there is no tribal language of their own. Most of them are illiterates and their social life reveals their traditional pattern of living. They live in thatched huts. They drink liquor and toddy heavily. Their staple food is rice.

Means of communication to the tribal settlements are poor. Bullock carts are the sole means of transport. Some of the settlements are inaccessible even to bullock carts. Only a few settlements are connected by jeepable roads.

With an extensive fieldwork on 9 villages under the block, the materials for the present paper could be available. The survey included demographic data, morphological data with regards to anthropometric measurements and visual observations, while the genetic data comprised A B O blood groups, colour vision, P T C tasteblindness, hand clasping and arm

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folding, hypertrichosis of the ear, middle phalangeal hair and palmar dermatoglyphics.

There are some reports available in the literature with respect to some genetical characters among the Koya Dora (K.D.) tribe of Coastal Andhra Pradesh (Dronamraju and Meerakhan, 1963). However, no material could be available on Konda Reddi (K.R.) tribe of the same region.

The purpose of the present paper is, therefore, to report data on some genetic markers among the two tribes mentioned above.

Materials and Method

The present paper comprise the following:

1. A B O Blood Groups and Tasteblindness.
2. Hand clasping and Arm folding.
3. Hypertrichosis of the ear.
4. Colour vision, and
5. Mid-phalangeal hair.

While data on genetic demography and morphological data with respect to anthropometry and visual observations and dermatoglyphics will be reported elsewhere.

The A B O Blood Group determination was done on 527 individuals, representing both groups and two sexes (K.R. = 227 and K.D. = 300), according to standard methods (Lawler and Lawler, 1957; Race and Sanger, 1962). Anti-sera was available from the Decrutz Co., Bombay. For Tasteblindness the sorting technique of Harris and Kalmus (1949) was followed.

The sample for hand clasping and arm folding consists of 364 individuals of both the tribes and of two sexes (K.R. = 163; K.D. = 201). The pattern of clasping the hands (or folding the arms) presents two alternative positions according to which thumb (or arm) occupies the upper portion: the right thumb (or arm) – type R, and the left thumb (or arm) – type L (see Freire-Maia et al, 1958; Winchester, 1958, Pons, 1961).

Hypertrichosis of the ear was observed only on 265 male subjects (K.R. = 132; K.D. = 133), due to its established Y linkage. The method described by Stern et al (1964) has been followed.

The subjects studied for colour vision comprise 678 individuals, 386 males, and 292 females of both tribes (K.R. = 216; K.D. = 170). Ishihara (1960) plates from number 18 to 24 were used to test all these subjects.

Mid-phalangeal hair data were collected from 512 individuals belonging to two sexes and tribes (K.D. = 235; K.R. = 277).

The heterogeneity χ^2 were calculated using the G tables of Woolf (1957) and probability levels were obtained from Fisher and Yates tables (1953).

Results

A B O Blood Groups and Tasteblindness

Table 1 shows the distribution of A B O Blood Group frequencies among the two tribes, K.R. and K.D. It is apparent from the table that both in K.R. and K.D. the blood group "O" occurs in the highest frequency followed by A, B and AB in the order. No significant difference could be observed either between the tribes or within the tribes (sexes), when heterogeneity χ^2 value for the tribes were considered. Examining the tribes of Hyderabad, Mac-Farlane (1940) detected high frequency of "B" among the Adi-Hindus (untouchables) with "O" in the second order. However, the Banjara tribe (Mac-Farlane, 1940) showed high "O" and very low "AB".

In Tasteblindness both K.R. and K.D. is characterized by a higher frequency of tasters than non-tasters (Table 2). No significant difference could be observed within the sexes. However, when the two tribes were compared the frequency of non-tasters were increased in the former, presenting a weakly significant heterogeneity Chi-square value ($\chi^2 = 6.364$, for 1 d.f.) with a 5% level of probability.

TABLE 1

Distribution of ABO Blood Groups among Konda Reddi and Koya Doras

Population	No. investigat-ed	Percentage 0	A	B	AB	Allele Frequencies p	q	r	p+q+r	D	χ^2	P
K.R. :												
M	127	39.38	28.34	23.62	8.65	0.207	0.112	0.680	1.000	0.012	0.058	0.90
F	100	45.00	32.00	18.00	5.00	0.206	0.122	0.671	1.000	0.000	0.0003	0.99
M+F	227	41.85	30.40	21.14	8.87	0.206	0.150	0.643	1.000	0.002	0.0006	0.99
K.D. :												
M	174	39.65	26.44	22.99	10.92	0.211	0.189	0.599	1.000	0.025	0.019	0 99
F	126	34.92	34.92	23.81	6.35	0.237	0.165	0.596	1.000	0.012	0.004	0.99
M+F	300	37.67	30.00	23.33	9.00	0.22	0.178	0.602	1.000	0.01	0.052	0.99

Heterogeneity Chi-Square (with 3.d.f.) = 1.562 ($P<0.70 - 0.50$)

K.D = Koya Dora, K. R = Konda Reddi, M = Male, F = Female

TABLE 2

Distribution of Tasters and Non-tasters (Taste-blindness) among K.R. & K.D.

Population	No. investigated	Tasters		Non-tasters		Gene Frequency		χ^2
		No.	%	No.	%	T	t	
K.R. :								
M	140	113	80.71	27	19.29	0.54	0 46	0.00023
F	88	68	77.27	20	22.72	0.52	0.48	$P<0.99$
M+F	228	181	79.39	47	20.61	0.53	0.47	for 1 d.f.
K.D. :								
M	217	185	85.26	32	14.74	0.62	0.38	1.8352
F	142	128	90.15	14	9.85	0.69	0.31	$P<0.10$–0.20 for
M+F	359	313	87.19	46	12.81	0.65	0.25	1.d.f.

Heterogeneity Chi-square = 6.364 for 1.d.f. $P<0.05$
Significant

Hand clasping and Arm folding

Table 3 gives the distribution of the type of hand clasping and arm folding among K.R. and K.D. tribes. It is significant to note that in both the groups the percentage of "L" individuals exceeds that of "R" individuals in hand clasping. And the same pattern is also observed in arm folding. It is apparent from the above observations that the incidence of "L" trait for hand clasping and arm folding among males and females of both groups show homogeneous distribution for this trait.

Hypertrichosis of the ear

Previous studies report that the tribal population exhibits the lowest frequency of this trait (Chakravartti, 1968). In this present study also the percentage of the affected with hypertrichosis pinnae auris presents the lowest frequency (Table 4). When compared with the available data from Andhra Pradesh (Dronamraju, 1961), the present data presents a slightly higher incidence (K.R.=9.84% ; K.D.=10.52%) of the trait against 6.1% of Dronamraju (1961).

Colour-blindness

Table 5 shows the incidence of colour-blindness among the two tribes of K.R. and K.D. It is evident from the table that both these tribes show very low incidence of colour-blindness. Dronamraju and Meerakhan (1963) also observed a low percentage of colour-blindness (2.5%) among the tribals. No significant difference could be observed regarding the heterogeneity of this trait between the two groups ($\chi^2=0.4957$; $P < 0.80$ to 0.70, for 1. d.f.). Out of 292 females tested none of them were found to be colourblind.

Mid-Phalangeal Hair

Occurrence of Mid-phalangeal hair in different populations in different frequencies has been confirmed by many authors (Danforth, 1921; Bernstein and Burks, 1942; Garn, 1950). Table 6 displays the frequencies of individual tribal groups (K. R. and K. D.), with and without middle phalangeal hair. It appears that the frequency of individuals with middle phalangeal hair varies from 27.27% (K. D.) to 29.24% (K. R.). χ^2 test fails to demonstrate significant difference, suggesting homogeneity in the occurrence of this trait among these two tribes.

TABLE 3

Distribution of Hand Clasping and Arm Folding among K.R. & K.D.

Population	N	Hand clasping: Right (R) No.	Hand clasping: Right (R) %	Hand clasping: Left (L) No.	Hand clasping: Left (L) %	Arm folding: Right (R) No.	Arm folding: Right (R) %	Arm folding: Left (L) No.	Arm folding: Left (L) %
K.R. :									
M	96	51	53.12	45	46.88	48	50.00	48	50.00
F	67	23	34.32	44	65.68	30	44.77	37	55.23
M+F	163	74	43.72	89	58.29	78	47.38	85	52.61
K.D. :									
M	131	56	41.99	75	58.01	71	54.20	60	45.80
F	70	27	38.57	43	61 43	32	45.72	38	54 28
M+F	201	83	40.28	118	59.72	103	49.96	98	50.04
	$\chi^2 = 0.6184$ for 1.d.f. $P < 0.70 - 0.50$					$\chi^2 = 0.4140$ for 1.d.f. $P < 0.80–0.70$			

TABLE 4

Frequency of Hypertrichosis of the Ear among the Males of K.R. & K.D. Tribes

Population	N	Present Abs.No.	Present %	Absent Abs.No.	Absent %
K.R.	132	13	9.84	119	90.16
K.D.	133	14	10.52	119	89.48
Total	265	27	10.18	238	89.82

Chi-square (with 1.d.f.) = 0.0332($P < 0.90$)

TABLE 5

Incidence of Colour-blindness among the Males of K.R. & K.D. Tribes

Population	N	Present		Absent	
		Abs.No.	%	Abs.No.	%
K.R.	170	5	2.87	165	97.12
K.D.	216	4	1.87	212	98.13
Total	386	9	2.37	377	97.62

χ^2 (Chi-square) = 0.4957, for 1.d.f. ($P<0.80-0.70$)

TABLE 6

Distribution of Middle-phalangeal Hair among the two Tribes of K.R. & K.D.

Population	N	Present		Absent	
		Abs.No.	%	Abs.No.	%
K.R. :					
M	153	50	32.68	103	67.32
F	124	32	25.80	92	74.20
M+F	277	82	29.24	195	70.76
K.D. :					
M	150	44	29.89	106	70.11
F	85	21	24.65	64	75.35
M+F	235	65	27.27	170	72.73

Heterogeneity Chi-square (χ^2) = 0.2345, for 1.d.f. $P< 0.90-0.80$.

SUMMARY

In a population genetic survey of the two major tribal groups K. R. and K. D. the data were presented on A B O Blood groups, P T C tasteblindness, hand clasping and arm folding, hypertrichosis of the pinnae auris, colour-blindness and mid-phalangeal hair.

1. The highest number of individuals among the two groups (K. R. and K. D.) belong to blood group "O" (K. R. = 41.85% ; K. D. = 37.67%). While the blood group "A" occurs in the next highest order (K. R. = 30.40% ; K. D. = 30.00%), followed by B, and A B in the subsequent order among the two tribes. The heterogeneity ($\chi^2 = 1.562$, for 3. d.f., $P < 0.70$) shows no significant difference.

2. Both in K. R. and K. D. the proportion of tasters outnumber the non-tasters. Significant difference has been observed with regard to the heterogeneity of the trait between the two groups.

3. The frequency of L-type of hand clasping persons is found to be 58.29% and 59.72% respectively among the K.R. and K. D. tribes. The same pattern is also observed in arm folding. The χ^2 shows homogeneous distribution for the trait in two groups.

4. The occurrence of hypertrichosis of the ear was observed among 9.84% of K. R. and 10.52% among K. D. tribes. Chi-square ($\chi^2 = 0.0332$, for 1.d.f., $P < 0.90$) test reveals homogeneity with regards to its incidence among the two tribes.

5. The relative frequency of colour-blindness among the males of K. R. and K. D. was observed as 2.87% and 1.87% respectively. No female was found to be affected.

6. It is observed from the data that 29.24% of K. R. and 27.27% of K. D. Subjects were found to have mid-phalangeal hair.

Finally, there appears to be very insignificant biological diversity between these two groups with regard to the above mentioned genetic traits. Studies specifically directed to test the assumption of homogeneity of populations are few but do

exist in the published literature which throw significant light on the problem either by showing demographically the occurrence of sub-populations within a population or by showing with genetic data variation between neighbouring communities or both (Nei and Imaizumi, 1966; Neel and Salzano, 1967; Basu, 1969). More studies specifically, designed for the purpose could solve many of our problems related to population genetical studies in India.

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A THEOREM ON RACE MIXTURE

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In population genetic studies, for all practical purposes, the estimation of gene frequencies largely depend upon the assumption of random mating. But it is to be noted that this assumption is quite serious since any deviation from it will attach no physical meaning to the estimates. To say it more explicitly let us consider the case of ABO blood groups. One may always equate the observed O, A, B and AB phenotypic proportions to r^2, p^2+2pr, q^2+2qr and $2pq$ respectively and solve for p, q, r subject to the condition $p+q+r=1$. But these solutions need not be the actual proportions in which A, B and O genes exist in the population unless the underlying population structure is of Model I (random mating) type. Moreover, it must be stated that whenever in a population ABO blood group phenotypes are seen in the above stated proportions, one should not declare that the population is under panmixia with respect to ABO blood groups with A, B and O gene frequencies given by p, q and r respectively. In this paper our contention is to prove a theorem showing that such a declaration will often be erroneous and hence should always be carefully avoided. It may be worth noting that though the main result is proved here in connection with the ABO blood group system, but it can easily be extended to any pheno gram analysis where the genotypes are not all distinguishable from one another.

THE THEOREM

Before proving the main result, let us first recall the set-up of Wahlund's effect (Yasuda, 1966) and see how that is extended to multiple alleles by Li (1969). We know that in a population, consisting of k mendelian isolates each of which practices random mating with respect to a character expressed by two alleles A and a (whose frequencies in the ith isolate are

p_i and q_i, respectively), the frequencies of the three genotypes AA, Aa and aa are given by $p^2+\sigma^2_p$, $2pq-2\sigma^2_p$ and $q^2+\sigma^2_p$ respectively, where $p=\Sigma w_i p_i$, is the average frequency of A-gene in the population, σ^2_p=variance of the gene frequency (p) among the isolates, and w_i=relative size of the ith isolate. We may note that $\sigma^2_p=\sigma^2_q=-\sigma_{pq}$ (since for all $i=1,2,\ldots, k$; $p_i+q_i=1$).

With three alleles A_1, A_2, A_3 (frequencies p_i, q_i and r_i respectively) the genotype frequencies in the population can be designated as follows:

$$\begin{array}{cccc} & A_1 & A_2 & A_3 \\ A_1 & p^2+\sigma^2_1 & pq+\sigma_{12} & pr+\sigma_{13} \\ A_2 & pq+\sigma_{12} & p^2+\sigma^2_2 & qr+\sigma_{23} \\ A_3 & pr+\sigma_{13} & qr+\sigma_{23} & r^2+\sigma_{33} \end{array} \left.\vphantom{\begin{array}{c}1\\1\\1\end{array}}\right\} \quad (1)$$

where, $\acute{o}^2_1=\Sigma w_i p^2_i-p^2$. sis the variance of A_1 gene frequency among the isolates and $\acute{o}_{12}=\Sigma p_i q_i w_i-pq$, is the covariance of the frequencies of A_1 and A_2, etc. Li (1969) has, further, shown that these variances and covariances are related on account of the restriction $p_i+q_i+r_i=1$. In fact, all the covariances may be expressed in terms of the variances

$$2\sigma_{12}=\sigma^2_3-\sigma_1{}^2-\sigma^2_2$$
$$2\sigma_{13}=\sigma^2_2-\sigma^2_1-\sigma^2_3$$
$$2\sigma_{23}=\sigma^2_1-\sigma^2_2-\sigma^2_3$$

Moreover, for each row of (1), one has

$$\sigma^2_1+\sigma_{12}+\sigma_{13}=O$$
$$\sigma_{12}+\sigma^2_2+\sigma_{23}=O$$
$$\sigma_{13}+\sigma_{23}+\sigma^2_3=O$$

In case of ABO blood groups since there is dominance relationship between the alleles A, B and O, replacing the A_1, A_2 and A_3 alleles by A, B and O respectively one has the proportions of the four phenotypes as

O......$r_2+\sigma^2_r$
A......$p^2+2pr+\sigma^2_p+2\sigma_{pr}$
B..... $q^2+2qr+\sigma^2_p+2\sigma_{qr}$
and AB......$2pq+2\sigma_{pq}$

The variances and the covariances, in this case, satisfy the relations

$$2\sigma_{pq}=\sigma^2_r-\sigma^2_p-\sigma^2_q$$
$$2\sigma_{pr}=\sigma^2_q-\sigma^2_p-\sigma^2_r$$
$$2\sigma_{qr}=\sigma^2_p-\sigma^2_q-\sigma^2_r$$

Again remembering that p, q and r are the averages of the quantities lying between O and 1, one has

$$\sigma^2_p\leq p(1-p),\ \sigma^2q\leq q(1-q) \text{ and } \sigma_{pq}\leq p(1-q) \text{ or } q(1-p)$$

$$\left.\begin{aligned}\text{Now put}\quad r_*&=\sqrt{r^2+\sigma^2_r}\\ p_*&=\sqrt{(p+r)^2+\sigma^2(_p+_r)}-\sqrt{r^2+\sigma^2_r}\\ &=\sqrt{(p+r)^2+\sigma^2_q}-\sqrt{r^2+\sigma^2_r}\\ \text{and}\quad q_*&=\sqrt{(p+r)^2+\sigma^2(_q+_r)}-\sqrt{r^2+\sigma^2_r}\\ &=\sqrt{(q+r)^2+\sigma^2_p}-\sqrt{r^2+\sigma^2_r}\end{aligned}\right\}\ (2)$$

One gets from (2),

$$r^2_*=r^2+\sigma^2_r$$
$$p^2_*+2p_*r_*=p^2+2pr+\sigma^2_p+2\sigma_{pr}$$
$$\text{and}\quad q^2_*+2q_*r_*=q^2+2_qr+\sigma^2_q+2\sigma_{qr}$$

Now if $p_*+q_*+r_*=1$, then

$$\begin{aligned}2p_*q_*&=1-(p^2_*+q^2_*+r^2_*+2p_*r_*+2q_*r_*)\\ &=1-[(p^2_*+2p_*r_*)+(q^2_*+2q_*r_*)+(r^2_*+\delta^2_*)]\\ &=2pq+2\sigma_{pq}[\text{ since } \sigma^2(_p+_q+_r)=O].\end{aligned}$$

Conversely, if $2p_*q_*=2pq+2\sigma_{pq}$, then $p_*+q_*+r_*=1$.

Thus we complete the proof of the theorem stated as follows :

A mixture of random mating races with average A, B and O gene frequencies p, q and r respectively cannot be distinguished from a homogeneous random mating population with gene frequencies p_*, q_* and r_* respectively, if and only if $p_*+q_*+r_*=1$
where, $p_*=\sqrt{(p+r)^2+\sigma^2_q}-\sqrt{r^2+\sigma^2_r}$, $q=\sqrt{(q+r)^2+\sigma^2_p}-\sqrt{r^2+\sigma^2_r}$
and $r_*=\sqrt{r^2+\sigma^2_r}$.

An Illustration

To make the picture a more concrete one let us consider the following example. Consider a population which is, in fact, a mixture of two mendelian isolates where the A, B and O

gene frequencies are 0.0300, 0.1688, 0.8012 and 0.5700, 0.1488, 0.2812 respectively. Assuming that the relative sizes of these two isolates are 0.5 and 0.5, one has the averages A, B, O gene frequencies for the whole population as

$$p=\frac{0.03+0.57}{2}=0.3000$$

$$q=\frac{0.1688+0.1488}{2}=0.1588$$

and

$$r=\frac{0.8012+0.2812}{2}=0.5+12$$

But, without knowing exactly this fact, if we proceed to obtain the gene frequencies by Wiener's formula (Wiener et al, 1929), we obtain $p_*=0.25$, $q_*=0.15$ and $r_*=0.60$ under the assumption of random mating. Thus a mixture of such two isolates will depict the same phenotypic frequencies as depicted by a homogeneous random mating population with, of course, different gene ratios.

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ON THE DETECTION OF F FROM ABO BLOOD GROUP DATA

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In view of the current interest in the problem of detecting inbreeding magnitudes in natural populations, the present article presents some investigations on similar lines. This problem made a beginning with an article of Ward and Sing (1970, unpublished: department of Human Genetics, University of Michigan, Medical School). Their problem was 'what should be the minimum sample size required to detect a given magnitude of F, from data on an autosomal character that involves no dominance relationship among its alleles'. The parameter F ($0 \leq F \leq 1$) measures the deviation from random mating. We consider the same problem with reference to ABO blood group data, and thus dealing with characters that involve dominance relationships. The basic line of approach is through a consideration of the power of the non-central χ^2 test to detect deviations of phenotypic proportions from Hardy-Weinberg proportions.

Let n denote the sample size and p, q, r denote the gene frequencies of A, B and O. Table 1 presents the phenotypic proportions both under Hardy-Weinberg equilibrium (Model – I) and deviation from it (Model – II).

TABLE 1

Phenotype	Proportion under Model – I	Proportion under Model – II
O	$\pi_1^* = r^2$	$\pi_1 = r^2 + Fr(1-r)$
A	$\pi_2^* = p^2 + 2pr$	$\pi_2 = p^2 + Fp(1-p) + 2pr(1-F)$
B	$\pi_3^* = q^2 + 2qr$	$\pi_3 = q^2 + Fq(1-q) + 2qr(1-F)$
AB	$\pi_4^* = 2pq$	$\pi^4 = 2pq(1-F)$

From Table 1 we can write

$$\pi_i = \pi_i^* + \frac{C_i}{\sqrt{n}} \quad : \quad i = 1, \ldots\ldots, 4.$$

where, C_i's are known functions of n, F and the gene frequencies. To detect any deviation from the Hardy-Weinberg proportions (under Model – I), one employs a non-central χ^2 test, whose non-centrality parameter is given by (Chapman, 1968)

$$\lambda = \sum_{i=1}^{4} C_i^2 / \pi_i^*$$

$$= n\ F^2 \left[2pq + (1-r)^2 + \frac{p(q-r)^2}{p+2r} + \frac{q(p-r)^2}{q+2r} \right]$$

It may be noted that this χ^2 distribution has only one degree of freedom. Tables giving the probability points for the limiting non-central χ^2 distribution determined by λ and having 1 d.f are tabulated by Owen (1962). Thus, for any combination of α(level) and β(power) of the test, λ can be directly read from the tables. Hence, the above equation for λ involves only two unknowns, once we fix a particular combination of values for p and q (r=1-p-q). Table 2 presents the (F, n) combinations for $\alpha=0.05$ and for suitable values of β and the gene frequencies. For example, to detect F=0.001 from a population with p=0.15, and q=0.15, at $\alpha=0.05$ and $\beta=0.9$. We need a sample of size 54,301,666. This study tells us that it is practically impossible to detect F in the neighbourhood of zero, due to our limitations on sample size. Worse still, if we are to detect it from a small isolate (required sample size exceeding the isolate size).

TABLE 2

($\alpha=0.05$)
p=0.15, q=0.15

F	$\beta=0.2$	$\beta=0.5$	$\beta=0.9$
0.0001	640,666,666	1,984,000,000	5,430,166,669
0.0005	25,626,666	79,360,000	217,206,666
0.0010	6,406,666	19,840,000	54,301,666
0.0050	256,266	793,600	2,172,066
0.0100	64,066	198,400	543,016
0.0500	2,562	7,936	21,720
0.1000	640	1,984	5,430
0.2500	102	317	868
0.5000	25	79	217
1.0000	6	19	54

F	β=0.2	p=0.20, q=0.20 β=0.5	β=0.9
0.0001	434,000,000	1.34,400,000	3,678,500.000
0.0005	17,360,000	53,760,000	147,140,000
0.0010	4,340,000	13,440,000	36,785,000
0.0050	173,600	537,600	1,471,400
0.0100	43,400	134,400	367,850
0.0500	1,736	5,376	14,714
0.1000	434	1,344	3,678
0.2500	69	215	588
0.5000	17	53	147
1.0000	4	13	36
		p=0.20, q=0.25	
0.0001	365,747,899	1,132,638,655	3,100,008,403
0.0005	14,629,915	45,305,546	124,000,336
0.0010	3,657,478	11,326,386	31,000,084
0.0050	146,299	453,055	1,240,003
0.0100	36,574	113,263	310,000
0.0500	1,462	4,530	12,400
0.1000	365	1,132	3,100
0.2500	58	181	496
0.5000	14	45	124
1.0000	3	11	31

F	β=0.2	p=0.25, q=0.25 β=0.5	β=0.9
0.0001	310,000,000	960,000,000	2,627,500,000
0.0005	12,400,000	38,400,000	105,100,000
0.0010	3,100,000	9,600,000	26,275,000
0.0050	124,000	384,000	1,051,000
0.0100	31,000	96,000	262,750
0.0500	1,240	3,840	10,510
0.1000	310	960	2,627
0.2500	49	153	420
0.5000	12	38	105
1.0000	3	9	26

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RIDGE COUNT IN PALMAR DERMATOGLYPHICS

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The papillary ridges on the palm, finger, sole and toes are formed very early in the foetal life, and except growing in size, remain unaltered throughout the life of an individual. Besides their permanency, there is no vague methodological problem in their counting as is the case in the formulation of palmar main lines, calculation of the main line index, etc. (Chatterjee & Chattopadhyay '69 ; Chattopadhyay '70). Hence they are a great asset in genetical and anthropological research. Unfortunately, studies on palmar ridge counts were neglected for a long time until Fang ('50) studied the inheritance of the a-b ridge count. He suggested that the a-b ridge count is due to a pair of allelomorphic genes, the gene for "high value" (when the ridge count of the two palms added together is above 78) is dominant over the one for "low value" (ridge count of the two palms added together is 78 or below). Pons ('64) concluded that the a-b ridge count is due to polygenes with additive effect. Tiwari ('66) and Pateria ('70) is in agreement with Pons ('64). Mitra et al ('65) failed to confirm Fang's ('50) hypothesis that the high value is dominant over the low value. They stated that it could be due to polygenes as Pons ('64) suggested which may act singly or together producing differential a-b ridge count. They concluded that since there is continuous distribution of the countable values is present it is arbitrary to classify individual a-b ridge counts into two or a few alternative types.

Glanville('65 a, b) concluded that the a-d ridge count and the ridge counts of patterns of the interdigital areas of the palm are genetically controlled and a polymeric system with genes of additive effect is responsible for this trait.

Basu & Chattopadhyay ('67) from their study of twins found that the MZ twins are far more highly correlated than

the DZ twins for a–b, a–c, a–d, b–c, b–d and c–d ridge counts which suggest that they are determined by heredity.

Chattopadhyay ('68) showed that the inter digital triradial ridge counts a–b, a–c, a–d, b–c, b–d and c–d are very highly correlated with one another (the correlation coefficients has been found to vary from 0.43 to 0.89). From this he concluded that the inter digital triradial ridge counts are determined by the same set of genes. The possibility that they are due to different sets of genes seems to be quite remote.

Though the exact mode of inheritance of the ridge counts in palmar dermatoglyphics is still unknown, it is interesting to note that the ridge counts show variation from one population to another.

Besides their importance as an anthropological marker for studying population variation, ridge count has been found to discriminate between normals and individuals with Down's syndrome (Fang, '50; Berg, '67). Holt and Turral's ('62), study did not substantiate the above finding. Holt ('63), Holt & Lindsten ('64) however, found that cases with aberrant sex-chromosomes show significant defferences in a–b count from comparable control populations.

a–b Ridge Count

The a–b ridge count in different populations are given in Table 1. It is evident that the a–b ridge count is usually high among the populations of Europe and America (79.64–84.88) as compared to those of India (76.92–80.25). The Anglo-Indians of India, a hybrid population of Indo-European origin, show a mean a–b ridge count of 81–71, which, incidentally, is intermediate between the Europeans on one side and the Indians on the other. The three Mongoloid populations, namely, the Ladhakis, Bhutanese and the Tibetans, do not conform to any definite pattern in this respect. The Ladhakis are found to be close to the other Indian populations, while the Tibetans resemble the Europeans for the a–b ridge count. The Bhutanese males show the lowest a–b ridge count reported so far. The difference between the two sexes has been found to be insignificant by most of the workers.

TABLE 1

Mean a-b Ridge Count in Some Populations

Population		Total Number	Mean	Investigator
	M	424	83.04±0.50	
	F	435	83.01±0.46	Fang, '50
	M+F	859	83.03±0.35	
English :				
Males	M	250	85.49±	
Females	F	250	84.88±	Holt & Turrai, '62
	M	77	86.25±1.20	
Ontario British	F	83	85.54±1.12	-do-
	M+F	160	85.88±0.81	
Ontario Indian	M	26	83.42±1.71	
(P. S.)	F	14	85.64±2.65	-do-
	M+F	40	84.20±1.35	
	M	29	80.00±1.70	
Ontario Indian	F	43	81.02±1.60	-do-
	M+F	72	80.51±1.16	
European	M	26	81.38±2.20	
Russian	F	38	80.16±1.57	-do-
	M+F	64	80.66±1.29	
	M	41	79.74±2.03	
European Jew :	F	27	79.98±1.50	-do-
(Polish)	M+F	68	79.84±1.35	
Bavarian	M	50	80.96± ?	Baitsch & Schwarzfisher, '59
	F	150	83.97± ?	
Spaniards	M	200	82.59±	Pons '61
	F	200	84.04±	
Swedish	M	39	87.85	
	F	50	82.54	Holt & Lindsten, '64

Indians :				
General Population of Andhra Pradesh	M	80	76.92±0.91	Dutta, '61
Binjhwar of Chattesgarh (M. P.)	M		69.10±0.86	Singhrol & Sen '71
	F		68.70±0.91	
General Population of the Panjab	M	62	76.42±1.58	
	F	38	80.68±1.47	Seth, '63
	M+F	100	78.04±1.14	
Purabia Chamars	M	46	71.92±1.38	
Gujar basis	M	42	68.19±1.45	Shrivastava & Rastogi, '67
General population of Maharashtra	M	72	82.89±0.65	
	F	73	76.82±0.93	Bansal, '66
Ladhakis	M	145	79.83±1.24	Dash Sharma, '66
	M	50	79.30±1.48	
Izhavas	F	50	75.66±1.73	Bhanu & Malhotra, '67
	M+F	100	77.48±1.21	
Bengalees :	M	104	77.22±1.05	
Rarhi Brahmins	F	60	77.61±1.19	Chattopadhyay & Dash Sharma, '66
Kayasthas	M	18	78.39±1.68	
	F	40	77.47±1.49	-do-
	M	6	72.16	
Baidyas	F	32	79.81±1.56	-do-
Bagdis	M	33	81.80±2.18	-do-
Duley	M	9	76.66	-do-
General population of Bengal (mostly Brahmins)	M	463	79.43	Mukherjee, '67
	F	371	79.33	
Bhutanese	M		70.1 ±1.09	Bhasin, '65
	M	100	84.07±1.18	
Tibetans	F	100	82.97±1.02	Chattopadhyay, '69
	M+F	200	83.52±0.80	

b–c AND c–d COUNT

The mean b–c and c–d counts are given in Tables 2 and 3 respectively. For both the traits the Maharashtrians are found to occupy an intermediate position between the Izhavas and the Bhutanese. For these ridge counts also the sex difference has been found to be insignificant. The highest mean b–c and c–d ridge counts are encountered among the Ladhakis.

TABLE 2

Mean b–c Count in Some Populations

Population		Total Number	Mean	Investigator
Izhavas	M	50	53.24±3.44	Bhanu & Malhotra, '67
	F	50	52.83±3.58	
	M+F	100	53.04±1.95	
Maharashtrians	M	65	49.03±1.15	Chattopadhyay, '67
	F	65	47.95±1.21	
	M+F	130	48.49±0.84	
Bhutanese	M	66	43.37±1.15	Bhasin, '66
	F	16	44.75±1.97	
Ladhakis	M	53	54.58±1.81	Dash Sharma, '68

TABLE 3

Mean c–d Count in Some Populations

Population		Total Number	Mean	Investigator
Izhavas	M	50	72.52±0.51	Bhanu & Malhotra, '67
	F	50	73.00±0.50	
	M+F	100	72.76±0.47	
Maharastrians	M	65	67.44±1.33	Chattopadhyay, '67
	F	65	67.14±1.01	
	M+F	130	67.29±0.84	
Bhutanese	M	70	58.94±1.43	Bhasin, '66
	F	16	59.18±1.80	
Ladhakis	M	53	74.13∓2.02	Dash Sharma, '68

a-d Count

The mean a-d ridge count in different populations are given in Table 4. The highest and the lowest counts are shown by the Ladhakis and the Bhutanese respectively. No sex difference has been found for this trait by the different workers; the only exception being the Izhavas (Malhotra & Bhanu, '67).

An interesting point observed is that the Punjabis and the Bhutanese, and the Maharashtrians and the Izhavas, though living quite apart, resemble each other for this trait. This is rather difficult to explain. It may be due to convergence.

Table 4

Mean a-d Count in Some Populations

Population		Total Number	Mean	Investigator
Izhavas	M	50	151.10±1.31	
	F	50	134.04±1.64	Malhotra & Bhanu, 67
	M+F	100	142.57±1.28	
	M	73	149.94±2.94	
Maharastrians	F	75	142.00±2.84	Chattopadhyay, '67
	M+F	148	145.16±2.14	
Rarhi Brahmins	M	103	151.57±2.89	
	F	61	153.78±3.96	Chattopadhyay & Dash Sharma, '67
	M+F	164	152.39±2.35	
	M	66	135.67±3.06	
Punjabis	F	38	137.66±4.35	Seth, '68
	M+F	104	136.39±2.53	
Saryupari Brahmins (U.P.)	M	70	136.88±3.43	
	F	30	145.60±6.06	Tyagi, '70
	M+F	100	141.24±2.08	
	M	74	132.17±2.49	Bhasin, '66
Bhutanese	F	17	129.11±6.21	
Ladhakis	M	53	171.43±4.76	Dash Sharma, '68

Beside a-b, a-d, b-c and c-d, a-c and b-d counts have been made, as far as I am aware, only on the Maharashtrians (Chattopadhyay, '67) and the Ladhakis (Dash Sharma, '68); t-d count by Mukherjee ('67) and Berg, ('68); and the a-d count on the Brahmins of Saugar by Muthal ('67) for anthropological purposes. The investigations done so far are still too inadequate and further studies should be attempted in different parts of the world on this aspect of palmar dermatoglyphics which has hitherto been neglected.

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TASTE SENSITIVITY TO PHENYLTHIOUREA AMONG THE KHASI OF NORTH-EAST INDIA

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Various Mongoloid tribes live in the North-Eastern part of India. The Khasi tribe is one of them. This tribe is very interesting for many reasons. They speak Mon-Khmer dialect of the Austro-Asiatic linguistic group. They are matriarchal people.

The Khasi tribe is divided into four divisions, viz. the Khasi proper, who are known as the Khyngrem, the Pnar or the Jaintia, the Bhoi, and the War. The Khyngrem live in the western region, while the Pnar occupy the Jaintia hills lying on the eastern side. The Bhoi inhabit the low hills towards the north and north-east of the area. The War are found on the slopes and the deep valleys towards the Souh.

Intermarriage among the four divisions is freely permissible. But in practice, intermarriage is not so frequent, because of isolation caused by geographical conditions and also because of social customs. In the bordering area where two populations live side by side, intermarriage takes place. The present data, however, have not been collected from such areas, but from the interior regions, where the populations are comparatively homogeneous.

The purpose of the present work is to study the taste sensitivity to phenylthiourea of the four divisions of the Khasi tribe. The data are analysed to find out inter-division relationship in respect of this characteristic. Secondly, the Khasi tribe has been compared with some other mongoloid populations.

Material and Method

In course of a genetic investigation done among the Khasi, a total of 838 individuals were tested for taste sensitivity towards phenylthiourea. The data consists of 222 Khyngrem (132 males and 90 females), 170 Pnar (80 males and 90 females), 210 Bhoi (120 males and 90 females) and 236 War (141 males and 95 females). The age of the subjects varies between 10 and 40 years. In the survey every possible care was taken to avoid the related persons. The data were mainly collected from the educational institutions.

The ability to taste and threshold levels were determined by the serial dilution method described by Harris and Kalmus (1949). A 0.13% phenylthiourea solution was first prepared with boiled tap water and then the serial dilutions were made.

Data and Discussion

The distribution of the taste thresholds among the Khyngrem, Pnar, Bhoi and the War, is shown sex-wise in Table 1. The same is presented in Figure 1. The distributions of the threshold are bimodal. The antimode falls between solutions 4 and 5. The antimodal values were taken for the separation of the tasters from the non-tasters.

Table 2 shows the number and percentage of tasters and non-tasters and their respective gene frequencies in the four divisions of the Khasi. The chi-square values reveal that the sex differences are not statistically significant. Therefore the two sexes have been pooled together.

TABLE 1

Distribution of Taste Threshold Among the Four Divisions of the Khasi

Sol. No.	Khyngrem ♂	Khyngrem ♀	Khyngrem Total	Pnar ♂	Pnar ♀	Pnar Total	Bhoi ♂	Bhoi ♀	Bhoi Total	War ♂	War ♀	War Total
< 1.	3	1	4	4	3	7	6	4	10	3	1	4
1.	7	5	12	3	3	6	5	3	8	5	4	9
2.	3	2	5	2	2	4	6	6	12	7	2	9
3.	2	1	3	2	2	4	4	2	6	3	2	5
4.	0	1	1	3	4	7	4	3	7	1	1	2
5.	5	2	7	1	0	1	2	1	3	3	3	6
6.	15	5	20	7	8	15	6	7	13	17	6	23
7.	60	40	100	10	9	19	11	9	20	58	32	90
8.	26	10	36	14	14	28	12	12	24	27	18	45
9.	3	15	18	16	19	35	19	17	36	7	10	17
10.	2	3	5	12	12	24	23	15	38	4	7	11
11.	1	1	2	2	8	10	16	7	23	1	3	4
12.	2	1	3	1	3	4	4	3	7	2	3	5
13.	1	1	2	1	2	3	2	1	3	1	2	3
14.	2	2	4	2	1	3	0	0	0	2	1	3
Total	132	90	222	80	90	170	120	90	210	141	95	236

TABLE 2

Number and Percentage of Tasters and Non-tasters Among the Four Divisions of the Khasi

		No.	Taster No.	Taster %	Non-taster No.	Non-taster %	Gene frequency T	Gene frequency t
Khyngrem:	Male	132	117	88.63	15	11.36	.663	.337
	Female	90	80	88.11	10	11.11	.667	.333
	Total	222	197	88.74	25	11.26	.665	.335
Pnar:	Male	80	65	81.25	15	18.75	.567	.433
	Female	90	76	84.44	14	15.55	.606	.394
	Total	170	141	82.94	29	17.06	.587	.413
Bhoi:	Male	120	93	77.50	27	22.50	.526	.474
	Female	90	71	78.88	19	21.11	.541	.459
	Total	210	164	78.09	46	21.90	.532	.468
War:	Male	141	122	86.52	19	13.48	.633	.367
	Female	95	85	89.48	10	10.52	.676	.324
	Total	236	207	87.71	29	12.29	.650	.350
Khasi:	Male	473	397	83.93	76	16.07	.600	.400
	Female	365	312	85.48	53	14.52	.619	.381
	Total	838	709	84.60	129	15.39	.608	.392

The frequency of non-tasters is somewhat higher in the Bhoi (21.09%) than in the other three divisions, namely, Pnar (17.06%), War (12.29%) and Khyngrem (11.26%). The chi-square values (Table 3) reveal that in respect of the incidence of tasters and non-tasters, the Bhoi are significantly different from the Khyngrem and the War. There is, however, no statistically significant difference between the Bhoi and the Pnar. When each of the four divisions is separately compared with the pooled data of the Khasi, it is seen that only the Bhoi significantly differ from the average Khasi. Thus the Bhoi stand somewhat apart from the average Khasi as well as from the other divisions, except the Pnar.

TABLE 3

Chi-square Values: Incidence of Tasters and Non-tasters

Populations	Chi-square values	Remarks
Khyngrem-Pnar	2.727	not significant
,, -Bhoi	8.899	significant
,, -War	0.238	not significant
Pnar-Bhoi	1.392	,,
,, -War	1.837	,,
Bhoi-War	7.282	significant
Khasi-Khyngrem	2.410	not significant
,, -Pnar	0.296	,,
,, -War	1.411	,,
,, -Bhoi	5.119	significant

The mean values of taste threshold in the taster groups of the four divisions are given in Table 4. The Bhoi mean (9.09±.13) is significantly higher than the means of the Khyngrem (7.59±.11) and the War (7.76±.11). In this respect the Bhoi are similar to the Pnar (8.80±.15), which also significantly differ from the Khyngrem and the War, the last two being similar to one another (Table 5).

TABLE 4

Mean Values of Taste Threshold of Tasters

Population	Mean ± S.E.
Khyngrem	7.59 ± .11
Pnar	8.80 ± .15
Bhoi	9.09 ± .13
War	7.76 ± .11
Khasi	8.22 ± .12

TABLE 5

t – test of Significance

Populations	Value of t	Remarks
Khyngrem-Pnar	6.54	significant
,, -Bhoi	8.80	,,
,, -War	1.09	not significant
Pnar-Bhoi	1.46	,,
,, -War	5.59	significant
Bhoi-War	7.81	,,

The position of the Bhoi in relation to the other three divisions as well as to the average Khasi is noteworthy. The present writer studied anthropometric characteristics (1967, 1970), ABO Blood Groups (1968), finger patterns (1962, 1969) and palm prints (1966) of the Khasi tribe. On analysis of these data, more or less similar results were obtained. The Bhoi significantly deviate from the other divisions as well as the Khasi tribe as a whole. The present finding is also in confirmity with the earlier results. Thus the Bhoi are separating from the Khasi group. They appear to have already formed a separate biological unit. This separating tendency is, to some extent, is seen in the Pnar also.

At the present state of our knowledge, it is not possible to give a definite explanation of this phenomenon. However, it can be said that the separating tendency may be due to isolation caused by geographical conditions and social factors. We may

think of drift, selection, inbreeding, miscegenation as operating factors among others.

COMPARISON

Ignoring the intra-tribal differences the four Khasi samples have been pooled together for the purpose of comparison. The pooled data have been included in Table 6, along with some other mongoloid populations. The taste ability of the Khasi was earlier studied by Miki et al (1960). They found 21.8% non-tasters among the Khasi as against 15.4% in the present sample.

TABLE 6

Frequency of Non-tasters Among Some Mongoloid Populations

Population	No.	Non-taster %	Investigator
Khasi (N.E. India)	838	15.40	Present study
Khasi ,,	317	21.8	Miki et al, 1960
Nokte ,,	271	13.7	Kumar, 1954
Riang ,,	401	16.21	Kumar & Shastry, 1961
Lepcha (Sikkim & N. India)	154	7.2	Miki et al, 1960
Tibetan (N. India)	401	14.71	Tiwari, 1966
Tibetan ,,	242	10.74	Sharma, 1967
Spitian ,,	125	12.00	,,
Lahauli ,,	314	12.73	,,
Tharu ,,		15.07	Srivastav, 1961
Chinese (Malaya)	50	2.00	Lugg & Whyte, 1956
Chinese (England)	66	10.63	Barnicot, 1950
Japanese (Brazil)	295	7.11	Saldanha, 1958
Japanese (Japan)	656	8.23	Tsuji, 1957
Malayan (Malay)		16.04	Thambapillai, 1956

Generally speaking, among the Mongoloids outside India, the frequency of non-tasters is slightly lower than that among the Mongoloids of North and North-East India. In the former

group the frequency ranges from 2.0% (Chinese: Lugg & Whyte, 1955) to 16.04% (Malayan), whereas in the latter group it varies between 7.2% (Lepcha) and 21.8% (Khasi: Miki et al). The Khasi of the present study with a frequency of 15.4% fall within the Mongoloid range.

In the other populations of India, the frequency of non-taster is higher than that in the Mongoloid populations. Among the Southern Pahira, tribal population, it is as high as 65.71% and in the Northern Pahira it is 41.55% (Basu et al, 1965). The same authors found 49.54% non-tasters among the Kurmi Mahato. High frequency of non-tasters is seen in two tribal populations of South India also: 43.44% in the Pallar and 47.34% in the Malapantram (Büchi 1955a, 1955b).

In the different caste groups of Uttar Pradesh the frequency of non-tasters varies from 24.6 to 38.8 (Srivastav, 1959). In the Garhwalis Brahmin and the Rajput the frequencies are 23.55 and 25.33 respectively (Tiwari & Bhasin, 1967).

From the Uttar Pradesh the number of non-taster individuals increase to Western and North-Western India. 44.5% of the Gujarati (Vyas et al, 1955), 43.58% of the Maratha (Sanghivi & Khanolkar, 1950), 31.98% of the Panjabi (Sharma, 1959) and 29.17% of the Sindhi (Khullar, 1966) are non-tasters. On the other hand in the non-tribal population of Southern and Eastern India the frequency of non-taster varies from 26.8% to 33.7% (Tiwari & Bhasin, 1967).

Summary

The Khasi form a mongoloid tribe of North-East India. They are divided into four divisions, namely, Khyngrem, Pnar, Bhoi and War.

Taste sensitivity to phenylthiourea of a Khasi sample comprising 222 Khyngrem, 170 Pnar, 210 Bhoi and 236 War (total 838) was studied. No statistically significant sex differences have been observed in the frequency of tasters and non-tasters. Intra-tribal analysis of the data reveals that the Bhoi significantly differ from the Khyngrem and the War as well as from the Khasi tribe as a whole, showing higher frequency of non-taster

individuals (21.9%). In the tribe the percentage of non-taster is 15.4.

With regard to this characteristic, the Khasi tribe has been compared with some other mongoloid populations. In general, among the mongoloid population the frequency of non-taster is low in comparison to that in the other populations.

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POPULATION BIOLOGY OF THE THREE SPLIT GAVDA GROUPS OF GOA

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INTRODUCTION

This paper is a preliminary report of the study on three endogamous split Gavda groups from Goa. Much of the detailed analysis remains to be completed, but enough is apparent at this stage to throw some light, we believe, on Prof. Karve's hypothesis regarding caste origins in India. In an earlier paper (Karve and Malhotra, 1970) results of some characters were presented.

THE POPULATION

The Gavdas who number about 1,20,000 (one lakh twenty-thousand) are found scattered throughout the Union territory of Goa. Most of them are farmers. They speak an Indo-Aryan language called Konkani, which is held by some scholars as a dialect of Marathi language. Although they eat fish, there is a taboo on eating chicken and eggs. They drink liquor heavily. Their staple food is rice and fish.

Around the year 1620 part of the Gavdas got converted into Christianity. This conversion has given rise to two endogamous groups from one breeding population. Interestingly enough during the period 1926–32 i.e., 40 years back part of the Christianized Gavda community was reconverted to Hinduism. This reconverted split group is known as Nav-Hindu Gavdas. The Hindu Gavda as yet do not consider Nav-Hindus as Hindus and therefore have no marriage reciprocity with the Nav-Hindu Gavdas. The three groups, namely, Hindu Gavdas, Christian Gavdas and Nav-Hindus thus represent three Mendelian populations, originated through fission, from one *panmictic* population. The spread of these three groups suggests that the two

splits must have taken place more or less at random. Collected genealogies show that the split took place at village and family level. The present (1969) population strength of these groups is as follows :

Hindu Gavdas	– 55,000
Christian Gavdas	– 35,000
Nav-Hindu Gavdas	– 30,000
Total*	1,20,000

The three split groups maintain strict endogamy and out of 240 marriages recorded, not even in a single instance the partner was sought from outside the group. The marriages are contacted both within the village as also outside the village. In 10% of the total marriages the partner was from the same village, where as in the rest the distance varied from 1 Km. to 64 Kms. with an average of little over 32 kilometres. Considering the length and breadth of the Goa territory, it seems that the marital alliance system is widely scattered among the Gavdas.

The Gavdas allow both matri-lateral and patri-lateral type of cross-cousin marriages. The incidence of consanguineous marriages is incorporated in Table 2. Of all the consanguineous marriages (42, 17.50%), 15% are of the matri-lateral type. It is interesting to note that although patri-lateral type of cross-cousin marriage is theoretically permitted, its actual incidence in all the groups is 0%. However, when the incidence of matri-lateral is considered for each group separately, it is significant to note that the Christian Gavdas have only 1.3%, while the Hindu Gavdas and Nav-Hindus have 23.61% and 19.78%, respectively. We are unable to explain this at the moment, but our enquiries with the Christian Gavdas showed that they continue to practise these preferential marriages.

*These figures have been obtained from the leaders of these groups and therefore are not entirely dependable. There was, however, no other source, through which these figures could be obtained. One thing, however, is certain that Gavdas collectively are the most numerous group in Goa.

The age at marriage for males varies from 18–25 years with an average of 20 years, and for females it varies between 15–19 years, with an average of 17 years. Although no data was collected regarding the average age of mothers at the birth of their children, as also the average age of all fathers, it can safely be guessed that since the Gavdas are highly illiterate and do not adopt to family planning methods, most of the females will get pregnant within a year of marriage. On this assumption the calculated average age of mothers at the birth of their children, and average age of all fathers will be around 19 and 22 years, respectively. Thus 20.5 years may be taken as the current length of generation. Therefore the first and second split in terms of generations took place about 17–18 and 2 generations ago, respectively.

Methods and Materials

A number of unrelated males from each of these split groups were studied for morphological characteristics and genetic traits. For the former males with no obvious physical deformity between the ages of 20 and 56 years were considered, and for the later males between 8 and 56 years were included. The subjects came from about 50 villages. The number of subjects studied for each of the trait is shown in Table 1.

The field work was organized through local officials, leaders and friends in both villages and schools. The entire data was collected in three field trips: November–December 1968, November – December 1969, January 1970.

Samples of blood were collected aseptically from the finger tips by pricking with the help of a Fraunek's needle. A few drops of blood were collected in a small test tube 90×10 m.m., containing about 2 c.c. of fresh normal saline solution. The samples were preserved in a large Thermosflask containing ice and were brought personally to Poona by Train and Bus. At Poona the blood samples were tested at Armed Forces Medical College. Part of the samples were flown to Calcutta and tested at the Indian Statistical Institute, under the supervision of Prof. S.R. Das.

In all 13 somatometric measurements, 13 visual characters and 8 genetic markers were recorded on each subject. Besides, rolled bilateral finger and palmar prints were recorded on each of the subject.

In taking measurements we have strictly adhered to the techniques recommended by Martin and Saller (1956). The techniques for blood grouping were those described by Race and Sanger (1954); for testing colour-blindness, that of Ishihara (1959); for identifying hypertrichosis of the ear, that of Malhotra (1969); and for tongue pigmentation, that of Rao (1970). The techniques followed for analyzing and collecting finger prints were those recommended by Cummins and Midlo (1961).

Choice of the Characters

Since basically in the present investigation it was sought to test how far genetic drift can bring in variation in gene frequencies of the split groups, traits with known simple genetic mechanism, as also with complex genetic background were considered. The former were selected because genetic drift and selection can operate on these traits more effectively. On the traits having polygenic inheritance the action of mutation and selection is very slow and in case of genetic drift, almost non-existent.

In evaluating the data it was considered (1) that the three split groups are in genetic equilibrium and (2) that the consanguineous marriages observed in the groups does not require any statistical adjustments. For evaluating inter-group differences 't' test and χ^2 statistics have been applied. The chi-squares were calculated by using the G-tables of Woolf (1957) and probability levels were obtained from Fisher and Yates (1953).

In this preliminary reports, however, results of analysis of 13 somatometric characters, 13 visual observations and 8 genetic traits will be discussed. The somatometric characters are; Stature, Auricular height, Head length, Head breadth, Minimum Frontal breadth, Bizygomatic breadth, Nasal height, Nasal breadth, Upper facial height, External orbital breadth, Inter orbital breadth, Orbito-nasal arc and Horizontal Circumference of the head; the visual traits are Hair line, Ear lobe

attachment, Darwin's tubercle, Cartilaginous lump at the back of the ear, Nasion depression, Nasion bridge, Nasion septum, Chin form, Cleft chin, Dental occlusion pattern, Handedness, Hand-clasping and Arm Folding, and the genetic traits are A:B O, M N, Rh blood group systems, ABH saliva secretion, colour-blindness, Hypertrichosis of the ear, and tongue pigmentation. Besides the basic analysis of the finger dermatoglyphics is also discussed.

Results and Discussion

Result and analysis of various characters is given in Tables 3 to 27. The morphological, genetic and finger dermatoglyphics data have been *dealt* with separately.

I. Somatometric Characters

It is interesting to note that the three split Gavda groups showed no statistical differences with respect to all the 13 somatometric characters considered except Inter-orbital breadth. For this character the pair Hindu Gavdas and Christian Gavdas differ at 5% level of probability.

II. Visual Characters

Basic analysis of all the 13 visual characters is presented in tables 5–12. These reveal certain interesting findings. Unfortunately the analysis of these traits in various age groups is as yet not completed values of chi-square for inter-group differences with respect to visual characters are set in Table 13. The results could be summarized as follows :

(a) For characters, Ear lobe attachment, cartilaginous lump at the back of the ear, Nasion depression, chin form, cleft chin, Handedness and Arm-folding, the three Gavda groups show homogeneous distribution.

(b) The three groups show heterogeneous distribution for Hair-line, Darwin's tubercle, Nasal bridge, Nasal septum, Dental occlusion pattern and Hand-clasping. In the case of Hand-clasping, Darwin's tubercle and Hair-line, the degree of

significance is quite high, while in the rest of the cases, they are significant at 5% level of probability.

(c) The group Hindu Gavda differs from Christian Gavdas in four characters, while it differs from Nav-Hindus in only three characters; and the pair Christian Gavdas and Nav-Hindu Gavda differ in three characters.

III. Genetic-Markers

(a) The three groups show homogeneous distribution for ABO (χ^2d.f. 6–10.915, p 0.05), MN(χ^2d.f. 4–2.20, p 0.5), and Rh(X^2d.f.–5.624, p 0.25) blood group systems.

(b) No statistical significant differences have been observed in the trait ABH secretion (Table 17) in the saliva ($\chi^2$2 d.f. – 2.16, p.70).

(c) While the three groups show homogeneous distribution for hypertrichosis of the ear (Table 19), Christian Gavdas differ from Hindu Gavda and Nav-Hindu Gavda with respect to colour-blindness (Table 18) and tongue pigmentation (Table 20).

IV. Finger Dermatoglyphics

(a) The three groups show homogeneous ditribution for the (Tables 22, 23 and 24) three principal pattern types – whorls, loops and arches (χ^2d.f. –3, Hindu Gavda × Christian Gavda – 5.12; Hindu Gavda × Nav-Hindu – 1.75; and Christian × Nav-Hindu – 5.72).

(b) The pattern intensity index (Table 27), arch whorl index and loop whorl index apparently show homogeneous distribution, although no statistics has been applied as yet.

(c) The occurrence of like finger-print types (Table 25) in the three Gavda groups is strikingly homogeneous (χ^2d.f.1; Hindu Gavda × Christian Gavda – 0.11, Hindu Gavda × Nav-Hindu Gavda – 0.14).

(d) The incidence of monomorphic hands (Table 26) is also very similar, being 46, 50 and 47% among the Hindu Christian and Nav-Hindu Gavdas respectively.

TABLE 1

Number of Subjects Studied for Various Characters in Three Endogamous Gavda Groups

Characters	Endogamous Groups			Total
	Hindu Gavda	Christian Gavda	Nav-Hindu Gavda	
1. Anthropometric Characters	100	100	100	300
2. Hair line	98	93	98	289
3. Ear lobe attachment	199	193	198	590
4. Darwin's Tubercle	192	191	195	578
5. Cartilagenous lump at the back of the Ear	100	93	97	290
6. Nasion Depression	99	97	99	295
7. Nasion Bridge	99	98	100	297
8. Nasion Septum	99	100	99	298
9. Chin form	99	100	99	298
10. Cleft chin	198	193	196	587
11. Dental Occlusion Pattern	189	192	190	571
12. Handedness	194	191	197	582
13. Hand-clasping	197	192	198	587
14. Arm-folding	100	91	98	287
15. A.B.O. Blood Groups	100	192	102	394
16. MN Blood groups	100	186	102	388

17.	Rh Blood groups	100	100	102	302
18.	ABH secretion in saliva	100	100	101	301
19.	Colour-blindness	134	95	116	345
20.	Hypertrichosis of the ear	91	98	99	288
21.	Tongue pigmentation	109	191	156	456
22.	Finger and palmar prints	100	104	98	302

TABLE 2

Distribution of Consanguineous and Non-Consanguineous Marriages Among Three Endogamous Gavda Groups

Endogamous Group	N	Unrelated		Distantly related		Maternal Uncle's Daughter		Father's Sister's Daughter		Sister's Daughter	
		No.	%	No.	%	No.	%	No.	%	No.	%
1. Hindu Gavdas	72	54	75.00%	1	1.39%	17	23.61%	0	0.00%	0	0.00%
2. Christian Gavdas	77	75	97.40%	1	1.30%	1	1.30%	0	0.00%	0	0.00%
3. Nav-Hindu Gavdas	91	69	75.82%	3	3.30%	18	19.78%	0	0.00%	1	1.10%
Total	240	198	82.50%	5	2.09%	36	15.00%	0	0.00%	1	0.41%

TABLE 3

Statistical Constants of the Measurements of Different Characters for the Three Split Groups of Gavdas

Split Groups	N	Mean	S.D.
1	2	3	4
1. Stature :			
H.G.	96	161.9	55.27
C.G.	99	160.7	48.88
N.H.	100	161.5	51.02
2. Auricular Height :			
H.G.	96	12.7	3.17
C.G.	99	12.1	2.52
N.H.	100	12.9	4.90
3. Head Length :			
H.G.	100	18.4	2.38
C.G.	100	18.5	2.64
N.H.	100	18.6	4.50
4. Head Breadth :			
H.G.	100	14.3	5.10
C.G.	100	14.0	4.79
N.H.	100	14.1	4.24
5. Minimum Frontal Breadth :			
H.G.	100	10.7	3.19
C.G.	100	10.5	3.42
N.H.	100	10.6	3.87
6. Bizygomatic Breadth :			
H.G.	100	13.30	1.94
C.G.	100	13.36	1.58
N.H.	100	13.31	1.89
7. Nasal Height :			
H.G.	100	4.5	1.20
C.G.	100	4.5	2.42
N.H.	100	4.5	1.61
8. Nasal Breadth :			
H.G.	100	3.7	2.25
C.G.	100	3.7	2.62
N.H.	100	3.7	1.89

1	2	3	4
9. Upper Facial Height :			
H.G.	95	6.29	3.19
C.G.	100	6.35	2.80
N.H.	98	6.27	3.11
10. Biorbital Breadth :			
H.G.	100	9.4	4.00
C.G.	100	9.2	3.20
N.H.	100	9.4	2.70
11. Inter Orbital Breadth :			
H.G.	100	3.1	1.04
C.G.	100	2.9	2.25
N.H.	100	3.0	2.00
12. Orbito Nasal Curve :			
H.G.	100	10.5	3.39
C.G.	100	10.1	3.92
N.H.	100	10.4	2.25
13. Horizontal Circumference of Head :			
H.G.	100	53.3	8.30
C.G.	100	52.9	5.23
N.H.	100	53.4	5:95

In short, the comparisons between the three groups reveal that:

(1) out of all the 13 somatometric characters, only one character inter-orbital breadth showed significant difference.

(2) six Visual characters out of 13 considered showed difference for at least one pair of endogamous groups.

(3) out of eight genetic traits considered, significant differences of low magnitude have been observed for two characters,

(4) various traits of finger dermatoglyphics showed homogeneous distribution.

(5) considering the individual pair of groups, the Hindu Gavdas differ in seven characters from the Christian Gavdas. while it differs only in three characters from the Nav-Hindus. The latter differs from the Christian Gavdas in five characters. Thus it seems that the Hindu Gavdas are more closer to the Nav-Hindus, than the Christian Gavdas.

Thus out of all the 38 traits considered in this study, significant differences have been observed in only nine characters.

TABLE 4

Obtained Values of 't' for Inter Group Comparisons with Respect to Somatometric Characters

Sl. No.	Characters	H. G. × C. G.	C. G. × N. H.	H. G. × N. H.
1.	Stature	0.1604	0.113	0.052
2.	Auricular height	0.146	0.102	0.339
3.	Head length	0.295	0.208	0.441
4.	Head breadth	0.449	0.156	0.381
5.	Minimum frontal breadth	0.411	0.188	0.251
6.	Bizygomatic breadth	0.304	0.618	0.117
7.	Nasal height	0	0	0
8.	Nasal breadth	0	0	0
9.	Upper facial height	0.130	0.0254	0.063
10.	Biorbital breadth	0.3904	0.4874	0
11.	Inter Orbital breadth	2.435*	1.017	1.217
12.	Orbito Nasal curve	0.772	0.652	0.246
13.	Horizontal circumference of head	0.407	0.797	0.959

*Indicates significant at 5% level of probability.

TABLE 5

Hair Line Types Among the Three Endogamous Gavda Groups

Endogamous Groups	No.	Widow's Peak Abs. No.	Widow's Peak %	Straight Abs. No.	Straight %	Irregular Abs. No.	Irregular %
Hindu Gavda	98	50	51.02	39	39.80	9	9.18
Christian Gavda	93	69	74.19	18	19.35	6	6.45
Nav-Hindu Gavda	98	49	50.00	31	31.63	18	18.37
Series Total	289	168	58.13	88	30.44	33	11.43

TABLE 6

Ear Lobe Types Among the Three Endogamous Gavda Groups

Endogamous Groups	No.	Soldered Abs. No.	Soldered %	Intermediate Abs. No.	Intermediate %	Free Abs. No.	Free %
Hindu Gavda	199	24	12.06	98	49.24	77	38.69
Christian Gavda	193	24	12.43	94	48.70	75	38.86
Nav-Hindu Gavda	198	23	11.61	84	42.42	91	45.95
Series Total	590	71	12.03	276	46.78	243	41.19

TABLE 7

Distribution of Darwin's Tubercle in Three Endogamous Gavda Groups

Endogamous Group	No.	Present R Abs. No.	Present R %	Present L Abs. No.	Present L %	Present R+L Abs. No.	Present R+L %	Absent Abs. No.	Absent %
Hindu Gavda	192	7	3.64	5	2.60	36	18.76	144	75.00
Christian Gavda	191	12	6.28	6	3.14	56	29.31	117	61.27
Nav-Hindu Gavda	195	7	3.59	3	1.53	36	18.47	149	76.41
Series Total	578	26	4.50	14	2.42	128	22.15	410	70.93

TABLE 8

Distribution of Cartilaginous Lump at the Back of the Ear Among Three Endogamous Gavda Groups

Endogamous Group	No.	Present R Abs. No.	Present R %	Present L Abs. No.	Present L %	Present R+L Abs. No.	Present R+L %	Absent Abs. No.	Absent %
Hindu Gavda	100	5	5.00	3	3.00	42	42.00	50	50.00
Christian Gavda	93	5	5.38	3	3.23	34	36.56	51	54.84
Nav-Hindu Gavda	97	3	3.09	4	4.12	40	41.24	50	51.55
Series Total	290	13	4.49	10	3.45	116	40.00	151	52.06

TABLE 9

Distribution of Nasion-Depression, Nasal Bridge and Nasal Septum Type Among Three Endogamous Gavda Groups

Endogamous Group	N	Nasion-Depression			N	Nasal-Bridge			N	Nasal - Septum		
		Shallow Abs. No. %	Medium Abs. No. %	Deep Abs. No. %		Straight Abs. No. %	Concave Abs. No. %	Convex Abs. No. %		Horizantal Abs. No. %	Upwards Abs. No. %	Downwards Abs. No %
Hindu Gavda	99	31	62	6	99	75	5	19	99	79	9	11
		31.31	62.63	6.06		75.76	5.05	19.19		79.80	9.09	11.11
Christian Gavda	97	22	63	12	98	82	9	7	100	79	12	9
		22.68	64.95	12.37		83.68	9.18	7.14		79.00	12.00	9.00
Nav-Hindu Gavda	99	23	67	9	100	85	9	6	99	83	14	2
		23.23	67.68	9.09		85.00	9.00	6.00		83.84	14.14	2.02
Series Total	295	85	183	27	297	242	23	32	298	241	35	22
		28.81	62.03	9.16		81.49	7.74	10.77		80.87	11.74	7.39

TABLE 10

Distribution of Chin Form and Cleft Chin Among the Three Endogamous Gavda Groups

Endogamous Groups	N	Chin Form: Prominent Abs. No.	%	Medium Abs. No.	%	Receding Abs. No.	%	N	Cleft Chin: Present Abs. No.	%	Absent Abs. No.	%
Hindu Gavda	99	12	12.12	79	79.80	8	8.08	198	35	17.68	163	82.32
Christian Gavda	100	7	7.00	82	82.00	11	11.00	193	32	16.58	161	83.42
Nav-Hindu Gavda	99	12	12.12	80	80.81	7	7.07	196	32	16.33	164	83.67
Series Total	298	31	10.40	241	80.88	26	8.72	587	99	16.87	488	83.13

TABLE 11

Dental Occlusion Types Among the Three Endogamous Gavda Groups

Endogamous Group	N	Edge to Edge Abs. No.	%	Over bite Abs. No.	%	Under bite Abs. No.	%
Hindu Gavda	189	22	11.64	167	88.36	0	0.00
Christian Gavda	192	11	5.72	178	92.71	3	1.57
Nav-Hindu Gavda	190	7	3.68	183	96.32	0	0.00
Series Total	571	40	7.00	528	92.47	3	0.53

TABLE 12

Distribution of Hand-Clasping, Handedness and Arm-folding Among Three Endogamous Gavda Groups

Endogamous Group	N	Hand-Clasping Right Abs. No.	%	Left Abs. No.	%	N	Handedness Right Abs. No.	%	Left Abs. No.	%	N	Arm-Folding Right Abs. No.	%	Left. Abs. No.	%
Hindu Gavda	197	111	56.35	86	43.65	194	183	94.33	11	5.67	100	50	50.00	50	50.00
Christian Gavda	192	111	57.81	81	42.19	191	176	92.15	15	7.85	91	54	59.34	37	40.66
Nav-Hindu Gavda	198	141	71.21	57	28.79	197	189	95.94	8	4.06	98	53	54.08	45	45.92
Series Total	587	363	61.83	224	38.17	582	548	94.16	34	5.84	287	157	54.32	132	45.68

TABLE 13

Values of Chi-square for Intergroup Differences with Respect to Visual Characters

Sl. No.	Character	D. F.	Endogamous Pair H. G.×C. C.	Endogamous Pair H. G.×N. H.	Endogamous Pair C. G.×N. H.
1.	Hair line	2	13.04[2]	3.98	7.66[1]
2.	Ear lobe attachment	1	0.02	2.26	2.06
3.	Darwin's tubercle	1	8.38[2]	0.10	10.41[2]
4.	Cartilaginous lump at the back of the ear	1	0.45	0.05	0.20
5.	Nasion Depression	2	3.56	1.98	0.56
6.	Nasion Bridge	2	7.22[1]	8.88[1]	0.11
7.	Nasal Septum	2	0.62	8.05[1]	5.07
8.	Chin Form	2	1.86	0.07	2.25
9.	Cleft Chin	1	0.09	0.00	0.13
10.	Dental Occlusion Pattern	2	8.22[1]	8.88[1]	5.11
11.	Handedness	1	0.73	0.55	2.53
12.	Hand-clasping	1	0.08	9.50[2]	7.68[2]
13.	Arm-folding	1	1.68	0.33	0.53

Statistical significance : 1 Significant at 5% level of probability
2 ,, ,, 1% ,, ,,
3 ,, ,, 0.1% ,, ,,

TABLE 14

Distribution of A-B-O Blood Groups in Three Split Groups of Gavdas of Goa

Split Groups	N		Incidence of phenotypes				Allele frequencies		
			O	A	B	AB	p	q	r
Hindu Gavda	100	obs.	40	34	21	5	0.219938	0.140382	0.639680
		Exp.	(40.92)	(32.98)	(19.93)	(6.18)			
Christian Gavda	192	obs.	56	63	54	19	0.243588	0.213170	0.543243
		Exp.	(56.66)	(62.21)	(53.19)	(19.94)			
Nav-Hindu Gavda	102	obs.	36	43	18	5	0.274240	0.120751	0.605009
		Exp.	(37.34)	(41.52)	(16.39)	(6.76)			
Total	394								

Chi-square (with 6 D.F.) = 10.915 ($P>0.05$)

TABLE 15

Distribution of M–N Blood Groups in Three Split Groups of Gavdas of Goa

Split Groups	N		Incidence of Phenotypes			Allele Frequencies	
			M	MN	N	m	n
1. Hindu Gavda	100	obs.	46	40	14	0.660000	0.340000
2. Christian Gavda	186	obs.	87	80	19	0.682796	0.317204
3. Nav-Hindu Gavda	102	obs.	51	43	8	0.710784	0.289216

Test of homogeneity yields $\chi_4^2=2.196$ ($P>0.5$)

TABLE 16

Distribution of Rh-Hr Blood Groups in Three Split Groups of Gavdas of Goa – Samples Tested with anti – C; anti – D; anti – E and anti – c

Split Groups	Number Tested		Number and per cent of phenotypes CCDee R1R1	CCdee R'R'	CCDEe R1RZ	CcDEe R1R2	CcDee R'r	Ccdee R'r	ccDEe R2r	ccDee Ror	CCdee rr
1. Hindu Gavda	100	No.	53	0	0	11	24	0	4	4	4
		%	53.00	0.00	0.00	11.00	24.00	0.00	4.00	4.00	4.00
2. Christian Gavda	100	No.	44	0	0	12	32	1	3	0	8
		%	44.00	0.00	0.00	12.00	32.00	1.00	3.00	0.00	8.00
3. Nav-Hindu Gavda	102	No.	60	0	0	10	25	1	1	3	2
		%	58.82	0.00	0.00	9.80	24.51	0.98	0.98	2.94	1.96

Test of homogeneity yields χ^2_6 d : f = 5.624 (P > 0.25)

TABLE 17

Incidence of Se-se Phenotypes and Gene Frequencies in the Three Split Groups of Gavdas of Goa

Split Groups	Number Tested		Number and per cent of Phenotypes SeSe and Sese	sese	Allele Frequencies Se	se
1. Hindu Gavdas	100	No.	80	20	0.85858	0.14142
		%	80.00	20.00		
2. Christian Gavdas	100	No.	72	28	0.83267	0.16733
		%	72.00	28.00		
3. Nav-Hindu Gavdas	101	No.	80	21	0.85613	0.14387
		%	79.21	20.79		
Total	301					

Test of homogeneity yeilds χ^2_2 d. f. $=2.16$ $(P>0.70)$

TABLE 18

Incidence of Colour-Blindness Among the Three Endogamous Gavda Groups

Endogamous Group	N	Absent		Present	
		Abs. No.	%	Abs. No.	%
1. Hindu Gavda	134	127	94.78	7	5.22
2. Christian Gavda	95	95	100.00	0	00.00
3. Nav-Hindu Gavda	116	111	95.69	5	4.31
Series Total	345	333	96.52	12	3.48

TABLE 19

Distribution of Hypertrichosis of the Ear Among Three Endogamous Groups of Gavdas

Endogamous Groups	N	Present		Absent	
		Abs. No.	%	Abs. No.	%
1. Hindu Gavda	91	32	35.16	59	64.84
2. Christian Gavda	98	41	41.84	57	58.16
3. Nav-Hindu Gavda	99	32	32.32	67	67.68
Series Total	288	105	36.45	183	63.55

TABLE 20

Incidence of Tongue Pigmentation Among the Three Endogamous Gavda Groups

Endogamous Groups	N	Present		Absent	
		Abs. No.	%	Abs. No.	%
1. Hindu Gavda	109	27	24.77	82	75.23
2. Christian Gavda	191	79	41.36	112	58.64
3. Nav-Hindu Gavda	156	40	25.64	116	74.36
Series Total	456	146	32.01	310	67.99

TABLE 21

Obtained Values for Inter-group Differences with Respect to Genetic Characters

S.No.	Genetic Trait	D F.	Endogamous pair H.G.×C.G.	Endogamous pair H.G.×N.H.	C.G.×N.H.
1.	Tongue Pigmentation	1	8.61[2]	0.03	9.55[2]
2.	Colour-blindness	1	7.66[2]	0.11	6.08[1]
3.	Hypertrichosis of the ear	1	0.89	0.17	1.91

Statistical Significance:

1. Indicates significant at 5% level of probability.
2. ,, ,, ,, 1% ,, ,, ,,
3. ,, ,, ,, 0.1% ,, ,, ,,

TABLE 22

Distribution of Three Galton Types among the Nav-Hindu Gavdas

Digits		Whorl	Radial Loop	Ulnar Loop	Radial+ Ulnar Loop	Arches
I.	No.	108	2	81	83	5
	%	55.10	1.02	41.33	42.35	2.55
II.	No.	104	22	53	75	17
	%	53.06	11.22	27.04	38.26	8.68
III.	No.	85	1	107	108	3
	%	43.37	0.51	54.49	55.10	1.53
IV.	No.	140	0	56	56	0
	%	71.43	0.00	28.57	28.57	0.00
V.	No.	67	0	128	128	1
	%	34.18	0.00	65.31	65.31	0.51
Total	No.	504	25	425	450	26
	%	51.43	2.55	43.36	45.91	2.65

TABLE 23

Distribution of three Galton Types among the Hindu Gavdas

Digits		Whorl	Radial Loop	Ulnar Loop	Radial+ Ulnar Loop	Arches
I.	No.	114	0	82	82	4
	%	57.00	0.00	41.00	41.00	2.00
II.	No.	97	18	74	92	11
	%	48.50	9.00	37.00	46.00	5.50
III.	No.	57	2	131	133	10
	%	28.50	1.00	65.50	66.50	5.00
IV.	No.	139	2	59	61	0
	%	69.50	1.00	29.50	30.50	0.00
V.	No.	82	1	117	118	0
	%	41.00	0.50	58.50	59.00	0.00
Total	No.	489	23	463	486	25
	%	48.90	2.30	46.30	48.60	2.50

TABLE 24

Distribution of three Galton Types among the Christian Gavdas

Digits		Whorl	Radial Loop	Ulnar Loop	Radial+ Ulnar Loop	Arches
I.	No.	116	2	87	89	3
	%	55.77	0.96	41.83	42.79	1.44
II.	No.	101	9	79	88	19
	%	48.55	4.33	37.99	42.32	9.13
III.	No.	62	1	139	140	6
	%	29.80	0.48	66.84	67.32	2.88
IV.	No.	130	0	76	76	2
	%	62.50	0.00	36.54	36.54	0.96
V.	No.	71	0	137	137	0
	%	34.13	0.00	65.87	65.87	0.00
Total	No.	480	12	518	530	30
	%	46.15	1.15	49.81	50.96	2.88

TABLE 25

Frequencies of Individuals who have pattern of the same type – Arches, Whorls, or Loops – on all the ten digits among three Endogamous Gavda Groups

Endogamous group	N	Like finger patterns on all ten digits		Unlike finger patterns on all ten digits	
		No.	%	No.	%
Hindu Gavdas	100	11	11.00	89	89.00
Christian Gavdas	104	13	12.50	91	87.50
Nav-Hindu Gavdas	98	14	14.28	84	85.72
Total	302	38	12.58	264	87.42

Although the significance of our findings is not very clear at the moment, pending detailed analysis of various characters, it is interesting to note that four characters, viz., colour-blindness, Tongue-pigmentation (Rao, 1970), Hair-line types and Darwin's tubercle are controlled by single genes; genetic mechanism for Nasal septum, Nasal bridge, Dental occlusion pattern and Inter-orbital breadth is as yet not determined, and Hand-clasping seems to have a doubtful genetic background. Further Hair-line types and Tongue-pigmentation are dependent on age (personal communication with D. C. Rao and Dr. R. L. Kirk).

It is now well established that the biological variation among the groups are caused by processes such as mutation, selection, migration, genetic drift and hybridization. In the present situation, however, since the three groups are sharing the same environment, have the same dietry habits, and the same pattern of mating behaviour the effect of selection should be non-existent. Since the splits have taken place only 17 and two generations ago, variations due to mutation must be negligible. Migration is not applicable in the present case and since the groups maintain strict endogamy, hybridization factor need not be considered. Consequently it seems that the differences are entirely due to genetic drift. However, it may be mentioned here that since the population size of these groups is fairly large, it is difficult to interpret the role of genetic drift. It is probable that after the degree penetrance of age dependent characters is calculated, the present interpretation may need suitable modification.

TABLE 26

Distribution of Monomorphic Hands in Three Endogamous Gavda Groups

Patterns		Hindu Gavda			Christian Gavda			Nav-Hindu Gavda		
		R	L	R+L	R	L	R+L	R	L	R+L
Whorl	No.	12	13	25	16	12	28	19	13	32
	%	12.00%	13.00	25.00	15.38	11.54	26.92	19.39	13.27	32.65
Loop Ulnar	No.	8	13	21	13	11	24	6	8	14
	%	8.00%	13.00%	21.00%	12.50	10.58	23.08	6.12	8.16	14.29
Total	No.	20	26	46	29	23	52	25	21	46
	%	20.00	26.00	46.00	27.88	22.12	50.00	25.51	21.43	46.94

TABLE 27

Frequency of Patterns & Indices Derived out of them in Three Endogamous Gavda Groups

Endogamous Groups	Whorls	RL	UL	RL+UL Total	Arch	P.I. Index	Arch-Whorl Index	Loop Whorl Index
Hindu Gavda	489	23	463	486	25	14.64	5.11	100.61
Christian Gavda	480	12	518	530	30	14.32	6.25	90.56
Nav-Hindu	504	25	425	450	26	14.87	5.11	112.00
Total	1473	60	1406	1466	81	14.61	5.50	100.48

This investigation, as it appears at this stage, supports our contention that the genetic heterogeneity observed in various endogamous groups, called castes or sub-castes in India, need not be due to genetic drift. This study thus gives further empirical support to I. Karve's hypothesis of caste origins.

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AN ESTIMATION OF THE Rh-NEGATIVE INCIDENCE IN THE BENGALI HINDUS

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INTRODUCTION

The simple dichotomy of the Rh blood group phenotypes into Rh-positives and Rh-negatives has still its importance in clinical obstetrics and blood transfusion. Keeping this importance in view the author has attempted to estimate the rate of Rh-incidence in the Bengali Hindus, based on the data so far available from various sources.

The author grouped 1135 blood samples (555 men and 580 women), from the Bengali Hindus with a single anti-D Rh serum.

The author has also compiled other published data on Rh blood groups on the Bengalis and compared the available series along with his own for homogeneity, which has been presented.

METHOD

The blood samples grouped by the author were tested by the tube method using the albumin replacement technique. The Rh serum was supplied by "Dade Reagents Inc., U.S.A." and by the "Blood Transfusion Service, Swiss Red Cross, Zurich". Table 1 shows the various sources from where the blood samples were collected. They were available from Calcutta and the district of 24-Paraganas, West Bengal. Blood was obtained either by vein puncture or by pricking the finger tip. Known positive and negative controls were included in each series of the tests.

Results

The results of the present series of 1135 bloods are given in Table 2, where sex-wise distribution of the Rh+ and the Rh−phenotypes has been shown. The sex-homogeneity chi-square estimated on a "2×2 contingency table" is found to be insignificant ($\chi^2=0.435$: 1 d.f. : P 0.50). The data for the two sexes have, therefore, been grouped together, which show an Rh+ incidence of 96.74% and an Rh−incidence of 3.26% in a population sample of 1135 Bengali Hindus.

Discussion

Several series of published Rh data for the Bengalis are available for a comparison (Table 3). The series 1 and 2 do not indicate about the religious affiliation, or castes, of the Bengalis. Series 3 offers data for Bengali Hindus, just as the present author's series (No. 4 in tables) without mentioning the castes. The series 5 to 10 and 12 to 16 specify the castes, of which the first six (5 to 10) could be grouped together under 'upper castes' and the latter five (12 to 16) under 'lower castes'.

The series 1 and 2 both for Bengalis are found to be very significantly heterogeneous ($\chi^2=12.195$, 1 D.F., $P>0.001$). The two Bengali Hindu series, Nos. 3 and 4, are found quite homogeneous ($\chi^2=0.0005$, 1 D.F.). The upper caste and the lower caste Hindu series, Nos. 11 and 17, are also found undifferentiated ($\chi^2=0.220$, 1 D.F., $P>0.50$). The four series, Upper caste Hindus (No. 11), Lower caste Hindus (No. 17), Bengali Hindus (Mitra et al, 1960, series No. 3) and Bengali Hindus (present study, series No. 4) have finally been tested for homogeneity by the 4/2 contingency table, yielding ($\chi^2=9.009$, 3 D.F., $0.05>P>0.02$) which indicates that these four series may be regarded as fairly homogeneous (heterogeneous at the 5% level, but not at the 2% level).

These four series of Rh data have been combined together, giving a total number of 224 Rh−negatives in a population of 7690 Bengali Hindus. *The incidence rate in the Bengali Hindus as estimated from the available consistent materials comes to 2.910% with a standard error of 0.192.*

TABLE 1

Sources of Bengali Hindu Blood Samples in the Present Study

	Source	No. Males	No. Females	Total No.
1.	Calcutta :			
1.1	Employees of Indian Statistical Institute	371	135	506
1.2	Patients of Institute of Child Health	93	39	132
1.3	Ante-natal Cases of Lady Dufferin Hospital	0	142	142
1.4	Patients of S.S.K.M. Hospital	39	17	50
2.	24 – Paraganas :			
2.1	Ante-natal Cases of R.K.M. Matri Mangal Hospital, Ariadaha	0	28	28
2.2	Students of Bhabanath Girls School, Kardaha	0	201	201
2.3	Students of Kinder-garten School, Shyamnagar	52	24	76

TABLE 2

Rh Positive/Negative Frequencies in 1,135 Bengali Hindu Males/Females

Sex	No. Tested	Rh-Positive		Rh-Negative	
		No.	%	No.	%
Male	555	535	96.396	20	3.603
Female	580	563	97.068	17	2.931
Total	1135	1098	96.740	37	3.259

The sex–Homogeneity Chi-Square (By '2 x 2' Table) = 0.435 Which is insignificant (1 D.F., P > 0.50).

TABLE 3

Distribution of Rh (D) Blood Group Antigen Amongst Various Hindu Bengali Populations in West Bengal

Sl. No.	Description of Population	No. Tested	Rh (D) No.	Positive %	Rh (D) No.	Negative %with	S.E.	Gene Frequencies D	Gene Frequencies d	Reference
1.	Bengalees	2200	2134	97.00	66	±0.36	3.00	0.8268	0.1732	(9)
2.	,,	1435	1359	94.70	76	±0.59	5.30	0.7698	0.2302	(8)
3.	Bengali Hindus	4448	4304	96.80	144	±0.83	3.20	0.8212	0.1788	(7)
4.	,,	1135	1098	96.74	37	±0.51	3.26	0.8194	0.1806	(present study)
5.	Bengali Hindu Brahmins	191	187	97.90	4	±1.03	2.10	0.8551	0.1449	(2)
6.	Bengali Hindu Rari Brahmins	254	248	97.64	6	±0.95	2.36	0.8464	0.1536	(3)
7.	,,	140	137	97.85	3	±1.22	2.15	0.8534	0.1466	(1)
8.	Bengali Hindu Kayastha	195	194	99.48	1	±0.50	0.52	0.9279	0.0721	(2)
9.	Bengali Hindu Dakshin Rari Kayastha	221	213	96.38	8	±1.25	3.62	0.8097	0.1903	(3)
10.	Bengali Hindu Vaidya	150	147	98.00	3	±1.14	2.00	0.8586	0.1414	(3)
11.	Upper Castes (Total of Sl. No. 5–10)	1151	1126	97.94	25	±0.41	2.06	0.8565	0.1435	—

12.	Bengali Hindu Uttar Rari Mahishya	200	192	96.00	8	±1.38	4.00	0.8000	0.2000	(3)
13.	Bengali Hindu Rajbangshi (Midnapur)	200	195	97.50	5	±1.11	2.50	0.8491	0.1581	(4)
14.	Bengali Hindu Rajbangshi (Jalpaiguri)	200	199	99.50	1	±0.48	0.50	0.9293	0.0707	(4)
15.	Bengali Hindu Rajbangshi (Coochbihar)	150	148	98.66	2	±0.94	1.34	0.8843	0.1157	(4)
16.	Bengali Hindu Tentulia Bagdi (Hooghly)	206	204	99.03	2	±0.68	0.97	0.9015	0.0985	(6)
17.	Lower Castes (Total of Sl. No. 12–16)	956	938	98.12	18	±0.43	1.88	0.8629	0.1371	—
18.	All Bengalees (Total of Sl. No. 1–10 and 12–16)	11325	10959	96.77	366	±0.02	3.23	0.8203	0.1797	—
19.	Bengalee Muslim (Hooghly)	221	217	98.19	4	±0.89	1.81	0.8655	0.1345	(1)

The highest and the lowest incidence rates of Rh-negative amongst the series of Bengali Hindus and the single Muslim series (No. 19) are found respectively in the Uttar Rarhi Mahishya (No. 12) showing 4% (in a sample of 200) and the Kayastha (No. 8) showing 0.52% (in a sample of 195). The latter series, however, very significantly differ from the rest except that for the Tentulia Bagdis (No. 16) which has a rate of 0.97%.

Expected rate of Erythroblastosis fetalis in Bengali Hindus

Estimation of the expected rate of Erythroblastosis fetalis in the Bengali Hindu population is done, on the basis of 2.910 per cent overall Rh-negative incidence rate.

Let p = freq. of D gene
q = freq. of d allele $[p+q=1]$

	Parent		*Child*
	0×0 ♂ +		
Genetype :	dd	Dd	$\frac{1}{2}$ dd + $\frac{1}{2}$ Dd
Probability	q^2	$2pq$ $(=2pq^3)$	$pq^3 + pq^3$
Genotype	dd	DD	Dd
Probability	q^2	p^2 $(=q^2p^2)$	$1p^2q^2$

Total pregnancies of Rh-negative mother:

Of these pregnancies —

(1) pq^3 will produces Rh (—ve) factors and the remaining
(2) $pq^3 + p^2q^2$ will produces Rh (+ ve) factors

Therefore,

(1.1) $$\frac{pq^3}{2pq^3 + p^2q^2} = \frac{q}{2q+p} = \frac{q}{1+q}$$ = Theoretical chances of Rh (—ve) mother having a pregnancy producing Rh (—ve) factors, i.e., completely safe.

And,

(2.1) $$\frac{pq^3+p^2q^2}{2pq^3+p^2q^2} = \frac{q+p}{2q+p} = \frac{1}{1+q} =$$ Theoretical chance of Rh (—ve) mother having a pregnancy producing Rh (+ve) factors.

Now $$\frac{1}{1+q} = \frac{1}{1+\sqrt{Rh\ (-\ )}} = \frac{1}{1+\sqrt{0.0291}} = 0.850 \text{ i.e., } 85\%$$

So in 85% cases of all pregnancies of Rh (—ve) mothers will have the genetic conditions for producing the Haemolytic disease of the foetus. From this it can be estimated that in 10,000 pregnancies 291 cases would be of Rh(—ve) mothers and of which 85% i.e., about 247 cases will have the Rh genetic conditions for Erythroblastosis fetalis.

Two reports (Stratton 1953 and Hartman 1949) estimated that the actual cases of Haemolytic disease of the foetus in the European population would occur at a much less frequency (about 5% to 10%) than what would be expected on the incidence rate of the Rh-incompatible matings. Assuming a similar rate of incidence in the Bengali Hindu population also, it is expected that only 12–25 cases in 10,000 pregnancies (5% to 10% of 247 mothers who are supposed to carry (Rh+ve) foetus) may actually manifest Erythroblastosis fetalis.

Summary

Results of testing a sample of 555 Bengali Hindu males and 580 females by the single Rh antiserum (Anti-D) have been presented and discussed. No sex-difference is revealed by these data. The combined total series of 1,135 Bengali Hindus have been compared with a number of published series relevant for the purpose. *An overall Rh-negative incidence rate of* 2.910 ± 0.192 *per cent has been estimated for the Bengali Hindus, based* on a total of 7,690 blood samples tested. Possible incidence rates of Haemolytic disease of new born in Bengali Hindus is also estimated and found to be about 12 to 25 cases in 10,000 pregnancies.

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A DIRECT FILTER PAPER TECHNIQUE OF BLOOD COLLECTION FOR STARCH GEL ELECTROPHORESIS STUDY OF LDH VARIANTS

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INTRODUCTION

Lactic dehydrogenase (LDH : E.C.1.1.1.27) is present in various tissues including erythrocytes in the mammals. LDH isozymes catalyze the reversible conversion of pyruvates to lactate in the chain carbohydrate metabolism. This enzyme is known to have genetic variants which can be demonstrated by Starch gel electrophoresis (Yakulis et al, 1962, Blake et al, 1969, Boyer et al, 1963). The incidence rates in populations so far surveyed are, however, very low (less than 1% to slightly above 4%), the highest incidence (4.14%) so far in the world has been found in the Nadar of Tamilnadu (India) reported by Ananthakrishnan et al, 1970.

For testing the LDH isozyme variants at least 0.5 ml. of blood is usually collected either in an anticoagulant or in clotted form and the erythrocytes are washed in isotonic saline for preparing haemolysates which are stored at below 0°C temperature until use. In mass surveys for LDH in haemolysates, even such a small quantity of blood is difficult to collect due to reluctance on the part of the donors. So a technique which would permit the LDH Starch gel electrophoresis studies using not more than a drop or two of capillary blood was felt urgently necessary. Such a simple technique has been tried with success by the present authors and forms the subject matter of the present paper.

THE NEW TECHNIQUE

In this method a small size filter paper strip is directly soaked with a drop of blood oozing out from the pricked finger

tip which cut into proper size is used as insert in the Starch gel electrophoresis. This direct filter paper technique is described below.

Three strips of 3 MM Whatman filter paper (3 cm./5mm.) were taken and one of the strips was soaked in buffer sol. (Na_2HPO_4 and Citric acid at pH 7.0 the buffer used for LDH gel and tank), another was soaked in dist. water and the third one was a blank. The excess of the fluid was squeezed out by pressing the strips in between two filter papers. Next, the three strips of filter paper were each soaked with a drop of blood obtained by pricking of finger tip.

Thus, blood samples from three persons including one person possessing the 'Calcutta-1' variant (Das et al, 1970) were taken in the above manner. A part of the blood from each person was also taken in 3.8% Na. citrate sol. to prepare the normal haemolysates to be used as control.

The blood-soaked filter paper strips were cut into proper sizes as inserts for Starch gel electrophoresis. Electrophoresis run of these inserts along with those of the haemolysates (as control) were carried out in the same gel following the method of Blake et al, 1969.

The rest of the blood-soaked filter paper strips were divided into three parts and were put into test tubes. One test tube was kept at the room temperature (about 30°C) and another was at 20°C and the third one was kept at 4°C in order to find out how long the LDH isozymes retain their activity in different temperature. The haemolysates were kept at 20°C.

After the electrophoresis run was completed, the LDH patterns were developed by reacting the gels with the substrate reagent (Blake et al, 1969).

The patterns obtained by the direct filter paper method did show no deviation from those produced by the control haemolysates. The intensities of the bands were also very similar.

A successive runs of electrophoresis using the pieces cut off from the blood-soaked filter paper strips which were kept at different temperature, were continued extending over a period from 16-4-1969 to 30-12-1969 in order to find out how long

the LDH isozymes retain their activities in dry filter paper, demonstrable by the Starch gel electrophoresis technique.

Thus four filter paper samples for three normal LDH and one 'Calcutta–1' LDH variant prepared from four donors gave persistant satisfactory zymograms for over a period of 90 days. Zymograms obtained after 105 days up to 123 days were appreciably faint. Three months after this stage, the bands were found not at all readable. It appears that LDH activity is retained *in the filter paper at 4°C* and can be most confidently identified in zymograms prepared *after 3–4 months* from the day of collection of the blood sample. Even those blood-soaked filter paper specimens which were kept at the room temperature (about 30°C) and at 20°C in the dry condition did not show any sign of deterioration within a period of 15 days. The high stability of LDH is certainly a contributory factor in the success of the present experiment.

The direct filter paper method described here has several practical advantages:

(i) Minimum quantity of blood, say one drop of blood is sufficient for the test; which is available from donors without much resistance.

(ii) Transportation of blood samples from the field to the laboratory is much easier (It is light, bottling problems or cooling problems avoided).

(iii) Test procedure is simple as the preparation of haemolysate is avoided.

(iv) Freezing temperature is not obligatory for preserving the blood samples for future use. Even at ordinary room temperature (about 30°C) for 15 days, the blood samples can retain their LDH activity.

SUMMARY

A new method using 3 MM filter paper strips has been devised for collecting blood samples for red cell LDH isozyme variants by Starch gel electrophoresis. The method has been found to be of significant advantage in mass screening of LDH variants present in erythrocytes.

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A STUDY OF ABO AND OTHER GENE FREQUENCIES IN TWIN CITIES OF HYDERABAD AND SECUNDERABAD

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INTRODUCTION

Populations differ in the frequencies of the genes concerned and presence or absence of certain alleles in a population makes it differ from other populations. The rather common occurrence of the gene which cause sickle cell anaemia in Africans and its absence or its extremely low frequency in Indians makes the two races differ. A knowledge of gene frequencies in a population sometimes may afford a knowledge of the relative incidence of certain disease patterns also. For example, the ABO blood group system is known to be associated with the incidence of peptic ulcers, duodenal ulcers and pernicious anaemia (Ford 1945, Clark 1955, Fraser Roberts 1959). Again non-tasters of phenylthiocarbamide (PTC) are likely to be more susceptible to development of adenomatous goitre (Harris and Kalmus 1949). Apart from its association with diseases, the ABO blood group system exhibits certain interesting properties like the segregation distortion and incompatibility of matings (Matsunaga & Itoh 1958, Matsunaga and Hiraizumi 1962 and Hiraizumi 1964).

The present paper gives the results of a sample survey made in the newly developing areas of the twin cities of Hyderabad and Secunderabad wherein most of the immigrants from Coastal Andhra and Tamilnadu had settled. The constitution of this population with respect to the genes at ABO blood group locus, PTC taste sensitivity and lobing of ears and factors influencing these gene frequencies have been examined.

Methods and Materials

In this study a random sample of 100 families were ascertained, the ancestors in case of most of the immigrant families (91) came from Coastal Andhra or Tamilnadu. These families came from different areas of twin cities namely, Malkajgiri, Kukatpally, Vidhyanagar, Ashoknagar, Chikadpally and Maredpally, wherein most of the immigrants had usually settled and thus are representatives of the newly developing areas of the twin cities. However, except for two Muslim families all others were Hindus.

A proforma was prepared to obtain information on ABO blood groups, PTC taste sensitivity (with 1% concentration), and lobing of ears of each individual of the family under study. Information concerning number of abortions, still births and number of dead children was also taken from each family. However, children who were not available at the time of study could not be included. It must be mentioned that only families with at least one living child were ascertained as this was a necessary stipulation for another study made simultaneously with this on these families.

From the hundred families a total of 521 individuals were tested for their ABO blood groups, 509 for PTC taste sensitivity (with 1% concentration) and 526 for the condition of lobing of their ears. This differential total number had arisen because certain young children below two years were not co-operative for blood group testing and certain others could not give proper answers about the taste of PTC.

The control group for the blood group distribution comprised the 10,251 donors (voluntary and paid) to the blood bank of Osmania General Hospital (Padma 1968).

The sample of 200 individuals with 100 females and 100 males studied by Grace Nirmala (1968) formed the control for PTC taste sensitivity.

Results

The distribution of the families according to their state of origin and caste (Brahmins & Non-Brahmins) have been given in Table 1 :

TABLE 1

	Brahmins	Non-Brahmins	Total
Tamilians	32	–	32
Andhras	39	20	59
Natives	1	8	9
Total:	72	28	100

The average number of living children per family was 4, the sex ratio among them being ♂ 1 : 1.08 ♀. The average number of children was higher in Brahmins (4.23) than in Non-Brahmins (3.32).

ABO GENE FREQUENCIES

The gene frequencies for ABO system of the control and the study group and its sub-groups (Brahmins & Non-Brahmins are given in Table 2. As was generally found in Indian populations (Neel and Schull 1966) we find that B group is more frequent than A, the O gene, however, having a frequency of order 0.5 – 0.6. The gene frequency of A blood group is similar in both control group and Non-Brahmins but significant differences exist with respect to B & O blood group gene frequencies. It is found that the gene frequencies of Brahmins ($\chi^2_2$2.78, 30.$<$P$<$, 50 are in equilibrium while those of study group (Total) (χ_3^2=14.794,.01$<$P$<$.001) and Non-Brahmins (χ_1^2=13.392,P$<$ .001) show a deviation from equilibrium.

Differences exist between gene frequencies of control and the study groups as evidenced by the heterogeneity test (χ_3^2=71.38, P$<$ .001). The Brahmins and Non-Brahmins also do not have similar gene frequencies, (χ_2^2=9.90, .01$<$ P$<$.001).

ABO INCOMPATIBILITY

The frequency of dead children and prenatal deaths did not differ significantly between compatible and incompatible couples (Tables 3 and 4). On the other hand there is an apparent increase of O children from ♀ O X A ♂ matings than from its reciprocal matings but the difference is significant at 10% level only (Table 5). It is also observed that incompatible matings

are significantly more than expected under random mating, the expected number being 8 while the observed number is 40. The data show a slight excess in the average number of living children from incompatible matings than from compatible matings (Table 3).

TABLE 2

Gene Frequencies of ABO Blood Groups

Blood group		O(r)	A(p)	B(q)	AB	Total
Control group	No. of individuals	4055	2204	3339	653	10251
	Gene frequencies	0.6304	0.1508	0.2188	—	1.0000
Study group	No. of individuals	155	119	167	80	521
	Gene frequencies	0.5197	0.2102	0.2701	—	1.0000
Brahmins	No. of individuals	103	103	118	59	383
	Gene frequencies	0.4995	0.2373	0.2632	—	1.0000
Non-Brahmins	No. of individuals	52	16	49	21	138
	Gene frequencies	0.5700	0.1404	0.2896	—	1.0000

TABLE 3

Average Number of Abortions and Deaths per Compatible and Incompatible Matings

	Compatible matings	Incompatible matings
Average number of abortions	0.426	0.65
Average number of dead children	0.213	0.40
Average number of living children	3.836	4.075

TABLE 4

Frequencies of Pre and Post Natal Deaths in Compatible and Incompatible Matings

Type of matings	Living children	Abortions	Dead children
Compatible matings	163	26	16
Incompatible	234	26	13
Total	397	52	29

χ^2 with one d.f for type of mating Vs Prenatal deaths = 1.5
χ^2 with one d.f for type of mating Vs Postnatal deaths = 2.209

TABLE 5

Segregation of O and A Children from A ♀ × O ♂ and O ♀ × ♂ A Matings

Type of mating ♀ × ♂	Offspring A	Offspring O	Total O	χ_1^2
A×O	21	8	29	
O×A	11	12	23	3.28
Total	32	20	52	

TABLE 6

Segregation of O and B Children from O ♀ × B ♂ and B ♀ × ♂ O matings

Type of mating ♀ × ♂	Offspring O	Offspring B	Total	χ_1^2
B×O	5	15	20	
O×B	17	21	38	2.168
Total	22	36	58	

PTC Taste-Sensitivity

The percentage of tasters in control group was 71.5% where as it was 59.3%, 62.0% and 85.0% in study group, Brahmins and Non-Brahmins respectively. The gene frequencies of PTC taste sensitivity for control, study group and for Brahmins and Non-Brahmins are given in Table 7.

Differences in the distribution of gene frequencies of control and study group is significant while Brahmins and Non-Brahmins are homogeneous with regard to their distribution the χ^2values being 9.08 (1 d.f., .01<P< .001) and 4.401 (2 d.f., .20 <P< .10) respectively.

Table 7

Gene Frequencies of PTC Taste Sensitivity

	Control group	Study group	Brahmins	Non-Brahmins
Tasters	143	302	253	67
Non-Tasters	57	207	144	63
Total	200	509	379	130
p	0.4662	0.3622	0.3837	0.3039
q	0.5338	0.6378	0.6163	0.6961

Ear Lobing

The percentage of individuals with free ear lobes are found to be 58%, 54.8% and 60.5% in study group, Brahmins and Non-Brahmins respectively. The corresponding gene frequencies are given in Table 8, and it is found that there is complete homogeneity between the genes distribution in Brahmins and Non-Brahmins, the χ_3^2 value being 1.39 (.20< P< .30).

When the association between blood groups, taste sensitivity and lobing of ears was examined, it was found that the blood group distribution did not differ either between the attached and free ear lobe groups (χ_3^2=6.99, .10<P< .05) or between tasters and non-tasters of PTC (χ_3^2=6.23, .20<P< .10) in spite of the fact that the male and female tasters differed in their blood group distribution (χ_3^2=2.1075, P> .90). It was found here' that female tasters possessing the B blood group

antigen (i.e. B+AB) were more than such males whereas this difference was not evident in males and females without the B antigen.

TABLE 8

Frequencies of Ear Lobing

Type of ear lobing	Study group Observed Nos.	Gene frequencies	Brahmins Observed Nos.	Gene frequencies	Non-Brahmins Observed Nos.	Gene frequencies
Free	296	p=0.3375	213	p=0.3274	83	p=0.3721
Attached	230	q=0.6625	176	q=0.6726	54	q=0.6729
Total	526	1.0000	389	1.0000	137	1.0000

DISCUSSION

Every population is characteristic in its genetic background and breeding structure. To that extent the selective forces that operate on each population might also be specific. Accordingly the present study group of individuals of the twin cities who are mostly immigrants from either coastal Andhra or Tamilnadu belonging to middle or upper middle classes in their economic position seem to exhibit certain features that are characteristic to them.

It is observed that the families studied have on the average about four children with a sex ratio of ♀ 1: ♂ 1. We find a slight distortion in the sex ratio of the sub-groups, female children being more common among Brahmins than in Non-Brahmins. It is however revealing to note that the average family size is much higher in Brahmins than in Non-Brahmins. This is obviously a reflection of the fact that Brahmins in general are conservative in their attitude to family planning and seem to have not yet fully responded to the necessity of reducing the family size. This appears to be especially so in the more well to do Brahmins as compared to corresponding well to do Non-Brahmins.

GENE FREQUENCIES

The estimation of gene frequencies with which various genes occur in the population is of significance. Since one can

characterise population in terms of the percentage representation of specific genes. The various genes considered now i.e., ABO blood group system, PTC taste sensitivity, and lobing of ear are of universal distribution and are observed in all populations studied so far.

ABO Blood Group System

The gene frequencies of the present study group are 0.5197, 0.2701 and 0.2102 for r, q and p respectively. Neel & Schull (1966) have given figures that are by far the most exhaustive and uptodate about the gene frequencies in the populations all over the world. It is observed that the gene frequency of B blood group is greater in the Northern India including Hyderabad and Secunderabad cities and areas much North. While the frequency of A gene is uniform in the entire country the B gene is more in North, than in South correspondingly the O gene frequency being less in North. This might explain the Aryan gene stock of the North and Dravidian gene stock of the South. However, twin cities which represent a fair admixture of Aryans, Dravidians and Muslims of Arabian origin also possess a higher frequency of B gene equal to that of North. Such a high value cannot be expected under the present degree of admixture of three races. An interesting point of the figures of Neel and Schull is that a majority of districts of the present Tamilnadu State have relatively higher frequency of B than the other districts of South India. The following table presents the approximate ranges of gene frequencies of the populations that now make up the present twin cities population.

Table 9

Gene Frequencies in Different Population Groups that make the Population of Twin Cities (Neel and Schull 1966)

S.No.	Population	O	A	B
1.	Twin cities and North India	.55 – .60	.15 – .20	.25 – .32
2.	Coastal Andhra	.60 – .65	.15 – .20	0 – .10
3.	Tamilnadu	.65 – .70	.15 – .20	.15 – .20
4.	Arabs	.70 – .75	.10 – .15	.15 – .20
5.	Study Group	.52	.21	.27
6.	Blood donors group	.63	.15	.22

As is evident from the above table the gene frequencies of twin cities do not reflect the fact that it is an admixture of the populations namely Andhras-Tamilians, Muslims of Arabian origin and North Indians in which case the gene frequencies in Hyderabad and Secunderabad should have been in the ranges .65–.70, .15–.20 and .15–.20 respectively of O, A and B. But there is an excess of the B gene in the population of twin cities at the expense of O gene. We may presume that this excess of B gene is due to some selective mechanism acting against O favouring B. Thus population groups who have migrated from Coastal Andhra and Tamilnadu might have been subjected to these selective forces. As we may see the gene frequencies of the present study group which consists mostly of immigrants from Coastal Andhra and Tamilnadu agree well with gene frequencies in twin cities as reported by Neel and Schull (1966) and thus provide strength to the argument. We may also quote Buettner-Janusch (1966) who states on page 419 that: "If B blood group is the result of a mutant gene in Asiatic populations, the relatively high frequency of the allele in such groups must be the result of very potent selection in its favour".

It is however, observed that the control group of blood donors constitutes a relatively higher frequency of O gene than of A and B and resembles with immigrant groups than the natives. Now it may be assumed that most of the donors come from poor native Telugu or Muslim families rather than from the other immigrant groups. There may then be two reasons for the apparent identity of the control gene frequencies with those of the immigrants. It may be that most of the donors are Muslims (i.e. Arabian immigrants) and the gene frequencies of these Muslims might have now attained a certain equilibrium at slightly lower frequency of O and higher frequencies of A and B than what the original levels of .70–.75, .15–.20, and .15–.20, were in the immigrants. It may also be that these Muslim immigrants may be only partly sensitive to the selective forces than the other immigrants and therefore their gene frequencies have not been altered to the same extent as other immigrant groups and thus we find in the control group somewhat intermediary gene frequencies between the native and the Muslim immigrants. A second reason may be that in view of several anaemias and diseases connected with blood groups,

one blood group may be more affected than the other thus reducing the frequency of donors of the more affected groups. In fact since most of the donors belong to poor families, there would be a greater chance for the expression of the deleterious conditions like anaemias or ulcers that are connected with one group or the other in these individuals. Consequently the donor group may not represent a true picture of the gene frequencies in the populations and hence the divergence of the control group from the actual frequencies.

Within the study group we note that Brahmins differ from Non-Brahmins, the reasons for which are not difficult to be understood because of the almost non-possibilities of exchange of genetic material between the two groups. We find that between Brahmins and Non-Brahmins most of the difference is in O and A frequencies B being almost same in both. The apparent equality of A gene frequency in the Non-Brahmin group and the control group may reflect the predominantly Non-Brahmin component in the control group of blood donors.

It is observed that the study group and the Non-Brahmins are not in equilibrium indicating the presence of selective machanism still functioning in the group. It is however, observed that the Brahmin group is in equilibrium. This may be due to sampling fluctuations, and if it is not, we must presume that the other groups also might attain these gene frequencies in due course.

ABO Incompatibility

Levine (1943) distinguished compatible pregnancies (or matings) where mother could safely receive a transfusion from the child (or father) from incompatible ones where she could not. The present data, however, do not provide any conclusive evidence for the presence of ABO incompatibility in the population concerned. First of all there are no significant differences in the prenatal deaths between com atible and incompatible matings (Table 4), but it may be argued that the sample is not large enough to reveal significant differences if any between the prenatal deaths. Moreover it is also true that the families ascertained were those with at least one living child and to that extent the absence of incompatibility may be due to the

failure of accounting for the childless marriages that may be obtaining in the population.

Notwithstanding these arguments, the conclusion of absence of incompatibility still seems to hold because the segregation of O and A & O and B from the corresponding compatible and incompatible matings do not show any distortion. The difference in the segragation of O and A individuals from compatible ♀ A×O ♂ and incompatible ♀ O× ♂ A matings was barely significant at 10% level (Table 6) and the difference between segregation of O and A children for the corresponding matings was not significant at all (Table 7).

However, Matsunaga and Itoh (1958) observed a deficiency of (A and B) children from the incompatible matings ♀ O× ♂ A (and ♀ O× ♂ B) in Japan. Further Matsunaga and Hiriazuni (1962) also showed that there is prezygotic selection of 'O' carrying sperms from AO×BO fathers. Thus the present group differs from the Japanese group.

PTC Taste Sensitivity

In the present study 40.7% of non-tasters and 59.3% of tasters were found in general in a sample of 509 individuals belonging to 100 different families. These showed a significant difference from an earlier sample of Grace Nirmala (1968) of 200n individuals ascertained at random where 28.5% were non-tasters and 71.5% were tasters. These differences may be due to differences in the communities that have made the two groups. We do not however know, what communities were making up the sample of Grace Nirmala.

From literature we find that the percentage of non-tasters is low in Mongoloids like Chinese, Japanese and Koreans and also in the Negroes of America, in the Negroids as in Kenya, Slaves of Alberta and American Indians. In the Caucasians we find it relatively high to very high frequency ranging from 30% in Zurich to 67% in Eskimos and Germans, Mohammedans and Arabs coming in between. We have one Indian sample of Gujars of Delhi (Seth et al, 1969) who have a very high per cent of non-tasters. The per cent sample also show a relatively high percentage of non-tasters ranging from 40% to 50% depending upon the communities.

In Brahmins the percentage of non-tasters is low but in Non-Brahmins it is relatively high. The apparently greater per cent of tasters among Brahmins than in Non-Brahmins may be due to the fact that Brahmins are not exposed to the same range of taste spectrum as the Non-Brahmins are. If there are certain related risks in the wider taste spectrum there will be some selection operating against tasters among Non-Brahmins. This is however, to be confirmed by rigorous observations.

Ear Lobing

We find that about 42% of the individuals have attached ear lobe and the frequencies of the genes are same in both Brahmins and Non-Brahmins. This indicates an identity of their genes and the possibilities of the same selective forces operating on the two groups. We, however, find that the present group shows a relatively higher frequency of attached ear lobes than Jats (18%) and Ahirs (31%) U.P., but much less frequency than Gujars (64%) of Delhi.

Summary

Gene frequencies at three loci viz. ABO groups PTC taste sensitivity and ear lobing were obtained from a sample of 100 families most of whom were immigrants from Coastal Andhra and Tamilnadu to the twin cities of Hyderabad and Secunderabad.

Analysis of data was made for the entire sample and for Brahmins and Non-Brahmins separately. On the average each family had about four chidren with sex ratio of ♂ 1 : 1.08 ♀. The average family size was higher in Brahmins (4.23) than in Non-Brahmins (3.32).

Gene frequency of the ABO blood groups were found to be $p=0.2102$, $q=0.2701$ and $r=0.5197$ respectively. When compared with other Indian groups and a group of blood donors, these gene frequencies exhibited differences which might be attributed either to sampling biases, selective forces or to the constituent community and racial differences.

There was no positive indication of the presence of incompatibility in the population. The gene frequencies of PTC as well as ear lobing did not show any obvious community differences.

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INCOMPATIBILITY LOAD DUE TO RH FACTOR IN SMALL POPULATIONS

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Introduction

The concept of genetic load was first developed by Haldane (1937) who considered it as the cost to a population's total reproductive potential for having genetic variation in fitness. In other words the deleterious alleles that segregate represent a sacrifice by the population for the struggle for existence in the process of achieving better adaptation. There are several kinds of genetic loads. Any force which changes gene frequencies can lead to a change in the average fitness and hence, with a certain amount of genetic variability, it leads to the expression of genetic load. A population subject to recurrent mutations decreases in average fitness and therefore exhibits a mutational load. This load is independent of the harmfulness of the mutant and is equal to the mutation rate for a recessive mutant and approximately twice the mutation rate for a dominant mutant. The same result was also obtained by Muller (1950) using an intuitive argument that each potentially dominant mutant leads, on the average, to one "genetic death" whereas if the mutant is recessive two mutant genes are eliminated with each extinction. Heterotic loci exhibit, on the other hand, a segregational or balanced load as described by Dobzhansky (1955). It may also happen that a genotype has a lowered fitness in association with certain maternal genotypes. A well-known example taken from Human genetics is in the case of a Rh+ child with a Rh- mother. In this case, the child may often die due to a hemolytic disease (*Ery-throblastosis fetalis*). The genetic load caused by this maternal-foetal incompatibility, is often called the incompatibility load. While in large populations the frequency of Rh-gene can come to a stable

equilibrium due to the recurrent mutations to this gene from the normal type, in small populations the gene frequencies drift away from the equilibrium points. This may result in the reduction in average fitness of the population and thereby creates a genetic load due to finite size of the population. As we shall see, in this paper, sometimes the genetic load may be negative implying an increase in the average-fitness.

The incompatibility load due to Rh factor involves selection against heterozygotes. However, selection here is not against the heterozygotes *per se* but only against those heterozygotes born to recessive mothers. Haldane (1942) and Li (1955) showed that such a situation leads to an unstable equilibrium. It was further remarked in the latter reference that a stable equilibrium can be produced when the loss of the deleterious gene is balanced by recurrent mutation to it from the normal type. In these studies the population is supposed to be so large that there are no random fluctuations in the gene frequencies. However, actual populations are finite and it is probable that the incompatibility load expressed in a small population may be drastically different from those expected in a very large population. Kimura *et al* (1963) discussed mutational load in a small population and obtained somewhat unexpected results such as dependence of the load on the harmfulness of mutant. The purpose of this paper is, therefore, to examine the incompatibility load created by a maternal-foetal incompatibility in the case of Rh-blood group in populations which are small in size.

Infinite Populations

In an infinite large population let there be three genotypes RhRh, Rhrh and rhrh for the Rh factor with rh gene recessive to Rh. Let the genotypic frequencies of these three genotypes are respectively p^2, $2pq$ and q^2 so that the frequency of rh gene is q. When the mother is recessive (Rh—negative) and her baby is heterozygous (Rh+positive), there often occurs the disease *Erythroblastosis fetalis* which may cause the death of the child. The heterozygotes born to recessive mothers have then lowered fitness which may be taken as $1-s$, whereas the remaining heterozygotes as well as all the homozygotes are normal having

fitness as 1. The situation is shown in Table 1 below reproduced from Li (1955) where we write 'A' for Rh and 'a' for rh.

TABLE 1

Selection Against Heterozygotes Born to Recessive Mothers

Mother X Father	Frequency	Child AA	Child Aa	Child aa	Total
AA X –	p^2	p^3	p^2q	0	p^2
Aa X –	$2pq$	p^2q	pq	pq^2	$2pq$
aa X AA	p^2q^2	0	$p^2q^2(-s)$	0	q^2-spq^2
aa X Aa	$2pq^3$	0	$pq^3(1-s)$	pq^3	
aa X aa	q^4	0	0	q^4	
Total	1.00	p^2	$2pq-spq^2$	q^2	$1-spq^2$

The change in the gene frequency of rh is then approximately $spq^2(q-\frac{1}{2})$, assuming s as small. If the initial value of q is below 0.5, the recessive rh gene will be reduced to a very low frequency in a few hundred generations. However, the occurrence of a relatively high frequency of this gene in the United States led Li (1955) to set up the hypothesis that there may be a very high mutation rate from Rh to rh which would compensate for the loss of the latter. If this mutation rate is denoted by u with no reversible mutation, the change in the gene frequency per generation is given by:

$$\triangle q = u\,(1-q) - \frac{s}{2}\,pq^2\,(1-2q) \qquad \dots \qquad \dots \qquad (1)$$

The equilibrium condition resulting by putting $\triangle q=0$ gives a cubic equation in q. However, if it is assumed that the initial value of q is rather small, the equilibrium frequency of rh gene is approximately given by:

$$q_e = \sqrt{\frac{2u}{s}} \qquad \dots \qquad \dots \qquad (2)$$

The change in the gene frequency in a particular generation then takes the form:

$$\triangle = q\frac{-s}{2}\,(1-q)\,(q+q_e)\,(q-q_e) \qquad \dots \qquad \dots \qquad (3)$$

This shows that the equilibrium is stable, the gene frequency gradually returning to the equilibrium point when disturbed in any direction for some reason. The average fitness of the population is, however, given by:

$$\overline{W} = 1 - 2u(1 - q_e) \qquad \ldots \qquad \ldots \qquad (4)$$

According to Crow (1958), the genetic load is defined as the proportion by which the fitness of the average genotype in the population is reduced in comparison with the best genotype. If the fitness of the best genotype is taken as 1, then the genetic load L_∞ is simply $1 - \overline{W}$. Hence this case.

$$L_\infty = 2u(1 - q_e) \qquad \ldots \qquad \ldots \qquad (5)$$

TABLE 2

Equilibrium Gene Frequency and Load in Infinite Population

s	$u = 10^{-5}$		$u = 10^{-6}$	
	q_e	L_∞	q_e	L_∞
0.001	·1413	1.72×10^{-5}	·0447	1.91×10^{-6}
0.01	·0447	1.91×10^{-5}	·0141	1.97×10^{-6}
0.100	·0141	1.97×10^{-5}	.0045	1.99×10^{-6}
0.500	·0063	1.99×10^{-5}	.0020	2.00×10^{-6}
1.000	·0045	2.00×10^{-5}	.0014	2.00×10^{-6}

The dependence of the gene frequency and load on the value of s and u are shown in Table 2. It is apparent that any increase in the disadvantage of the heterozygotes leads to an increase in the load, for example, with a lethal effect, $s = 1$ and with $u = 10^{-5}$, the load is about 2.00×10^{-5} whereas with $s = {\cdot}001$ and $u = 10^{-5}$ the load is about 1.72×10^{-5}. For large values of s resulting in low values of q_e the load is approximately 2_u.

FINITE POPULATIONS

In a finite population, the gene frequency will not be at its equlibrium value q_e because of the sampling which takes place in each generation. For very small population this may result

in fixation of the gene. However, this effect of sampling will be counter balanced by mutation tending to return the frequency to its equilibrium value. Consequently, the gene frequency will vary about this value over the generations and the genetic load, will also vary about its expectation. The interaction of mutation, selection and random drift due to sampling results in a probability distribution of gene frequencies which is in equilibrium and is independent of initial conditions. If we denote this distribution by $\phi(q)$, then $\phi(q)\,dq$ gives the relative frequency of populations having frequency of rh gene between q and q+dq. Wright (1938) gave a general formula for $\phi(q)$ given by:

$$\phi(q) = (C/V\delta_q) \exp\left[2\int (M\delta_q/V\delta_q)\,dq\right] \quad \ldots \quad (6)$$

where $M\delta_q$ and $V\delta_q$ are respectively the mean and the variance of the rate of change in q per generation and C is a constant such that the total area under the curve is unity.

In the present case we have, assuming a population of size N

$$M\delta_q = -(s/2)(1-q)(q^2 - q^2_e) \quad \ldots \quad (7)$$

$$V\delta_q = q(1-q)/2N \quad \ldots \quad (8)$$

This gives

$$\phi(q) = C \exp(-Nsq^2)\, q^{(2Nsq^2_e - 1)} (1-q)^{-1} \quad (9)$$

Since q is restricted to very small positive values and since $Nsq^2_e = 2Nu$ in view of (2), we have

$$\phi(q) = C \exp(-Nsq^2)\, q^{(4Nu-1)} \quad (10)$$

Such a distribution has the first three moments about the origin given by

$$\bar{q} = E(q) = \Gamma(2Nu+\tfrac{1}{2})/\sqrt{Ns}\,\Gamma(2Nu) \quad (11)$$

$$E(q^2) = 2u/s \quad \ldots \quad \ldots \quad (12)$$

$$E(q^3) = (2Nu+\tfrac{1}{2})\,\Gamma(2Nu+\tfrac{1}{2})/(Ns)^{3/2}\,\Gamma(2Nu) \quad \ldots \quad (13)$$

If Nu tends to 0, we can approximate these moments as below:

$$\bar{q} \simeq 2u\sqrt{(\pi N/s)} \quad \ldots \quad \ldots \quad (14)$$

$$E(q)^2 \simeq 2u/s \quad \ldots \quad \ldots \quad (15)$$

$$E(q^3) \simeq u\sqrt{(\pi/Ns^3)} \quad \ldots \quad \ldots \quad (16)$$

Assuming $u = 10^{-5}$, the mean gene frequency, $\bar{q}$ is shown as a function of N for a given value of s in Table 3.

TABLE 3

Mean Gene Frequency in Finite Populations with $u=10^{-5}$

N	s 0.001	0.010	0.100	0.500	1.000
10	0.0035	0.0011	0.0003	0.0002	0.0001
50	0.0079	0.0024	0.0008	0.0003	0.0002
100	0.0112	0.0034	0.0011	0.0005	0.0003
500	0.0250	0.0077	0.0025	0.0011	0.0008
1000	0.0354	0.0109	0.0035	0.0016	0.0011
5000	0.0790	0.0243	0.0079	0.0035	0.0025
10^4	0.1120	0.0344	0.0112	0.0050	0.0035
∞	0.1413	0.0447	0.0141	0.0063	0.0045

It is apparent from the results given in this table that the gene frequency in finite populations gets reduced considerably.

When the gene frequency is not equal to q_e, the mean fitness of individuals in the population is given by

$$\overline{W} = 1-sq^2(1-q) \quad \ldots \quad \ldots \quad (17)$$

The expected genetic load in finite populations is then obtained by taking the expectation of $L=1-\overline{W}$ with respect to the distribution ϕ (q). Hence

$$\begin{aligned}\overline{L} &= sE[q^2(1-q)] \\ &\approx 2u(1-\sqrt{\pi/4Ns}) \quad \ldots \quad \ldots \quad (18)\end{aligned}$$

This shows that the load is a function of u and Ns. It gives two very unexpected results. Firstly the load decreases with decrease in the population size. For very large values of Ns it is approximately 2u. As Ns decreases it also decreases below this value till it becomes 0 when $Ns=\pi/4$. Secondly, with further decrease in Ns it becomes negative. A negative genetic load means that the mean fitness is increased instead of being reduced.

With the help of (5) and (18), we can write

$$\overline{L} = L\infty\,[1-\sqrt{(\pi/4Ns)}]/(1-q_e) \quad \ldots \quad (19)$$

This shows again unexpectedly that $\overline{L}$, in general, will be less than L_∞, since q_e is expected to be smaller than $\sqrt{(\pi/4Ns)}$ in view of the fact that $Nu = Nsq_e^2$ is assumed to be approaching 0.

The dependence of the load on Ns is shown in Table 4, for $u = 10^{-5}$.

TABLE 4

Genetic Load in Finite Populations with $u = 10^{-5}$

Ns	$\overline{L}$
0.001	-54.00×10^{-5}
0.100	-3.60×10^{-5}
0.785	0.00
1.000	0.23×10^{-5}
2.000	0.75×10^{-5}
4.000	1.12×10^{-5}
8.000	1.37×10^{-5}
16.000	1.56×10^{-5}
32.000	1.69×10^{-5}
∞	2.00×10^{-5}

It is apparent from this table that in finite populations, the load is always less than 2u which serves as an upper limit. A comparison of the results given in this table with those in Table 2 shows that finite population loads are always smaller than those of the infinite populations.

DISCUSSION

The incompatibility load due to rh factor in small populations is due to the interaction of selection against heterozygotes born to recessive mothers, mutation to the rh factor and random drift. In very large populations, where random drift is practically absent, the forces of selection and mutation balance each other giving rise to a stable equilibrium. The load is due to the elimination of the rh factor in the form of heterozygotes. This appears to be a peculiar form of load which is

distinct from segregational load created by heterozygote advantage. It is more or less a type of mutational load created by the recurrence of the rh factor. If the equilibrium gene frequency q_e is small, the load is approximately twice the mutation rate. This result is similar to that of the mutational load due to a dominant mutant as shown by Haldane (1937). However, when a finite population is considered, the total load happens to be smaller than twice the mutation rate. It is also found to be negative for extremely small values of Ns. These results are quite unexpected and starting since the mutational load in small populations studied by Kimura *et al* (1963) were shown usually to be larger than their infinite population values. This could be due to the special type of selection considered in the context of incompatibility load. In finite population the gene is usually absent or fixed so that the elimination due to the heterozygosis is not likely to have a pronounced effect, thus leading to a smaller load and, in very small populations, even to a negative load.

Summary

The theory of the incompatibility load due to rh factor in a finite population has been developed. It is shown that this load is a function of the mutation rate and Ns. Contrary to expectations, the load is found to be smaller in small populations than in a large population. For extremely small populations the load could be negative implying that a random process could increase fitness instead of decreasing it.

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SICKLE CELL TRAIT AS GENETIC MARKER IN POPULATIONS

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INTRODUCTION

Sickle cell trait when first reported from India [(Lehmann and Cutbush 1952; Dunlop and Mazumdar 1952; Büchi 1955; Sukumaran et al, 1956), was considered to be present only in isolated pockets, without having much anthropological significance. However, the results of subsequent intensive search for the presence of the trait among a large number of populations, throughout India, repudiate the above belief. On the contrary Sickle cell trait is widely and systematically distributed in India, and its distribution closely follows the distribution pattern of certain groups of tribal populations (Negi, unpublished). In other words, from the point of view of anthropologist, Sickle cell trait provides a valuable marker in determining the genetic relationship between the major tribal populations of India.

Once acquired by a population, sickling gene would take centuries in a favourable environment for the heterozygote frequencies to rise to a considerable magnitude. Thereafter the gene will persist in the population for generations to come, as genetic marker, even if the selective advantage disappears, which will only result in the rapid fall in the frequencies up to a certain level. This according to Allison (1961) also, is the main value of the gene from anthropological point of view. Allison (1961) however, cautious against the attempt to use sickling frequencies to estimate the contribution of individual populations to mixed populations and is of opinion that in view of the powerful selection effects operating on the sickling gene the character connot be used for large-scale tracing of racial origins and movements. This objection may be true in case of diffusionist explanation to explain the occurrence of

sickle cell gene among diverse populations in widely separated areas of the globe. But in case of populations, otherwise known to have certain racial affinities and, living within a limited geographical area, the sickle cell gene can effectively be used to trace out population movements and origins. In the present paper, the distribution of sickle cell trait, in a large number of tribal populations, of non-mongoloid origin, and some lower caste populations, of India, is discussed in terms of genetic relationship between the populations.

Limitation of Malaria Sickle Cell Hypothesis

Before the discussion on the distribution of the trait is taken up a passing reference may be made regarding the validity of Malaria-Sickle cell hypothesis, which at present has a wide spread support. It is true that to a large extent the distribution of Sickle cell in India parallels the distribution of malaria. Yet there are certain limitations which question the validity of the Malaria-Sickle cell hypothesis in its entirety. In India not all populations living in highly malarial environment harbour the gene, besides there are marked variations, among the populations, in the frequencies of the trait enen through living in the similar or same environmental conditions. There are areas of very high malarial endemicity entirely free of sickling, whereas some populations harbouring the trait in high frequencies inhabit regions of low endemicity. As will be seen in the discussion that follows, the distribution of the trait in India has an ethnic basis and environmental conditions came into play to produce small variations among different segments of same populations, owing to the change in habitat.

The distribution of Sickle cell trait discussed in this paper is in respect of the non-mongoloid tribal populations of India inhabiting the geographical area South of Aravali, Vidhya and Rajmahal chain of hills. These populations variously known as Proto-Austroloid, Nishadic, Veddoid, Pre-Dravidians etc. comprise of major groups of tribal populations and cannot be grouped under a single classificatory term. In this paper the commonly used terms by which the various population groups are known are used to describe them.

INCIDENCE OF SICKLING IN 'GOND' GROUP OF POPULATIONS

The most numerous of these are the 'Gond' group of populations inhabiting the heart land of India from the Vindhyas in the north to the Godavari gorges in the South. The 'Gond' in the recent past were a dominant people and held their sway over a large area. Even now there are 'Gond' strongholds scattered far and wide in the central Indian region. 'Gondi' the language of 'Gond' belongs to Dravidian family of languages, but in many parts the 'Gond' seem to have forgotten their language and adopted the locally dominant language such as Chhatisgarhi or Hindi. In certain areas the Gond as a result of social advancement adopted the epithet 'Raj' to signify their superiority over the ordinary Gond, but the fact remains that the 'Gond' all over the central India region, in spite of the linguistic and social changes, are distinguishable from the other caste groups. Sickling is harboured by the Gond group of populations to a considerable magnitude as is apparent from Table 1.

TABLE 1

Distribution of Sickle Cell Trait among the 'Gond' Group of Populations

Sl. No.	Population	Locality	State	Sickling per cent
1.	Muria	Baster	Madhya Pradesh	13.46
2.	Maria	,,	,,	18.78
3.	Raj Gond	,,	,,	14.29
4.	Dorla	,,	,,	13.00
5.	Bhatra	,,	,,	16.07
6.	Gond	Bilaspur	,,	19.38
7.	Gond	Mirzapur	Uttara Pradesh	18.52
8.	Gond	Melghat	Maharashta	17.24
9.	Koya	East Godavari	Andhra Pradesh	16.95

From the distribution of the trait it is seen that the Gond group of populations uniformly harbour the gene ranging from 13 to 19 per cent. All these populations are scattered in a wide area and live in diverse environmental conditions.

From the distributional pattern there remains no doubt that the trait is a racial attribute of the 'Gond'.

Incidence of Sickling in 'Bhil' Group of Populations

The next numerous group is the 'Bhil' group of populations inhabiting Western India, just west of the Gond group. Unlike the 'Gond' the 'Bhil' group of populations have entirely lost their language and now speak Indo-Aryan languages. As regards the origin of 'Bhil' it is held that the term is derived from the Tamil word 'B–il' meaning bow, thus the population is known by the characteristic personal weapon, that is bow, of its men. If this be true then the 'Bhil' must have migrated north west to their present day habitat from their ancient habitat which must lie further South-ward in the peninsular region.

The distribution of Sickle cell in the Bhil group of population (Table 2) clearly indicates at least two distinct sub-groups. One having the higher frequency of the trait that is more than 20% and the other lower than 20%. The higher frequency of the trait is harboured by all those populations who regards themselves socially higher than the Bhil and each one of them is more or less a breeding isolate. The comparatively close breeding system in these populations gave rise to the increased frequencies of the gene from the lower frequency found in the larger populations known as simply 'Bhil'. The mechanism is however, not clear as to how these populations came to harbour the higher frequencies. The close breeding system must give rise to homozygosis and in case of sickling homozygosis will lead to elimination of the gene in greater magnitude, which must result in lowering the frequency rather than the increase. On the other hand, the argument of selective advantage in favour of heterozygotes in malarious environment, does not hold good in this case because the same advantage must also be available to the other populations, with lower frequencies, as they also share the same habitat, for almost the same number of generations. It must therefore be that the combined effect of close breeding system, in an environment offering selective advantage to heterozygotes resulted in higher frequencies of the gene in spite

of the selection against the homozygotes. It could be through greater fertility of heterozygote women or some other process which is yet to be studied.

TABLE 2

Distribution of Sickle Cell Trait Among the 'Bhil' Group of Population

Sl. No.	Population	Locality	State	Sickling per cent
1.	Dhanka	South Gujrat	Gujrat	23.08
2.	Bhil Vasava	,,	,,	26.60
3.	Gamit	,,	,,	23.53
4.	Chaudhra	,,	,,	26.09
5.	Paura	Dhulia	Maharashtra	24.55
6.	Bhil	,,	,,	15.85
7.	Garasia	Sirohi	Rajsthan	23.64
8.	Bhil	Banswada	,,	18.00
9.	Naik	South Gujrat	Gujrat	17.65
10.	Bhil Gameti	Udaipur	Rajsthan	9.77
11.	Bhil Dangi	Dangs	Gujrat	9.72

Apart from these intragroup variations, it is clear that the 'Bhil' as group harbour the trait in their genetic make up. In case the 'Bhil' came to the present habitat from South as it has been suggested, chances are great that there is a genetic relationship between the 'Bhil' and 'Gond' groups of population. The present day population boundaries which sharply demarcate the two groups, is rather an improbable phenomenon in case of populations. Besides bow is also as much a characteristic weapon of 'Gond' as that of 'Bhil'.

Absence of Sickling in Austric Speaking Populations

Munda or Kolarian group of populations inhabit the central and East central Indian region. The larger populations in this group are the Kol, Munda, Santhal, Kharia, Khairwar, Ho and Bhumij. Besides there are numerous smaller populations which may as well be the offshoots of the above mentioned large populations. It is a significant fact that the entire group is free from the sickle cell gene except sporadic cases here and

there which can very well be explained as intrusions from other populations (Negi unpublished; Kumar 1969; Bhattacharjee 1969; Kumar and Bhattacharjee 1969; Kumar and Mukherjee 1969; Bhattacharjee and Kumar 1969).

One departure from this characteristic absence of sickling in the 'Munda' group of populations is found in the Korku of Melghat forest in Maharashtra (Negi unpublished). The Korku who are Austric speaking tribe, are far removed from the other Austric speaking tribes, such as Kol and Munda. Instead they live in predominantly 'Gond' habitat. Thus the presence of sickling among the Korku (ca 9%) can well be explained as a result of admixture with the neighbouring 'Gond'. Sickle cell trait is, therefore, characteristically absent in the Austric speaking populations which has been referred here as 'Munda' group of populations, and in this regard are different from the 'Gond' and 'Bhil' group.

Incidence of Sickling in Tribal Populations of Southern India

The Southern tip of peninsula is inhabited by a number of small and interesting populations. It is in this region, this sickling was first reported in India (Lehman and Cutbush 1952). These findings were later confirmed by Büchi (1955), who also carried out his investigations among a number of populations South of Annamalai Hills, in the extreme South of Peninsula.

On the basis of distribution of Sickle cell trait (Table 3), the Southern populations can be grouped into three different groups. Firstly, the populations with moderate high frequencies of the trait; secondly, the populations with moderate frequencies and; lastly the populations entirely free of the trait. The total absence of sickling is in the Southern most tip of peninsula, South of Annamalai Hills. Büchi (1955) also did not detect the trait among a number of populations from this region. The absence of sickling among this group of population relates them to the Vedda of Ceylon, and if there are any true Veddoids in Southern India they can only be represented by these populations.

TABLE 3

Distribution of Sickle Cell Trait in South Indian Populations

Sl. No.	Population	Locality	State	Sickling per cent
1.	Malayali	Yercaud and Kolli Hills	Tamil Nadu	7.72
2.	Jenu Kurumba	Coorg	Mysore	2.80
3.	Betta Kurumba	,,	,,	8.33
4.	Yerara	,,	,,	23.70
5.	Adiyan	North Wynad	Kerala	32.00
6.	Kurumba	,,	,,	17.86
7.	Irula	Palghat	,,	20.27
8.	Muduga	,,	,,	6.00
9.	Paniyan	North Wynad	,,	21.53
10.	Kurchia	,,	,,	–
11.	Soliga	Coimbatore	Tamil Nadu	26.09
12.	Malasar	,,	,,	7.32
13.	Kadar	Annamalai Hills	,,	–
14.	Paliyan	Palni Hills	,,	–
15.	Pulayan	,,	,,	–
16.	Mannadiyar	,,	,,	–
17.	Kannikar	Trivandrum	Kerala	–

The populations with the high frequencies of the trait inhabit the region around Nilgiris. These populations probably belong to a distinct racial group, unrelated to the populations South of Annamalai. The third group of population having moderate frequencies are living in close proximity with the first group and share the same habitat. There can be no doubt in the fact that these populations got the trait from the first group and during the generation the trait registered some increase in a favourable environment.

SICKLING IN LOW CASTE POPULATIONS

Besides the tribal populations sickling is also found in some lower caste populations (Negi 1957, 1969; Das et al, 1967).

All such populations are of mixed origin and have tribal component in their genetic make up, in varying degrees. Sickle cell trait can be used to determine that component as it was found that only those low caste populations harbour the trait which live in proximity with the tribal populations, harbouring the trait. Besides there are regional variations in the frequency of the trait in the same population depending upon the presence and concentration of the tribal populations. This phenomenon is very well illustrated by the regional variations in the frequency of sickling in Mahar of various localities (Table 4).

TABLE 4

Distribution of Sickle Cell Trait in the Mahar Inhabiting Different Localities

Sl. No.	Locality	State	Sickling per cent
1.	Baster	Madhya Pradesh	38.21
2.	Nagpur	Maharashtra	18.66
3.	Dhulia	,,	13.04
4.	Thana	,,	11.76
5.	Kolaba	,,	5.79
6.	Aurangabad	,,	2.35
7.	Poona	,,	.55
8.	Ahmadnagar	,,	-
9.	Kolhapur	,,	-
10.	Satara	,,	-

The Mahar are distributed through out Maharashtra and a large part of Madhya Pradesh. They are at the lowest ladder of caste hierarchy and maintain the same status even in relation to various tribal populations of this region. Their peculiar social status has facilitated frequent admixture with various tribal elements. From the distribution of sickling among the Mahar it is seen that the frequency of the trait varies greatly in different localities, The highest frequencies are in Bastar and Nagpur which lie in the 'Gond' tract, followed by Dhulia, Thana, Kolaba, and Aurangabad in 'Bhil' tract. In Southern Maharasthra where there are no tribal populations sickling is also absent in the Mahar.

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ABO BLOOD GROUPS AND ABH SECRETION IN SALIVA OF BADE BHINJHWARS OF CHHATTISGARH

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During the winter months of 1970 a genetic survey was carried by some members of the Department of Anthropology, Ravi-Shankar University, Raipur, among the Bade Bhinjhwars of Chhattisgarh. Among other investigations, blood groupings and ABH secretion were also conducted among the Bade Bhinjhwars. The ABO and ABH secretion data and their analysis are presented in this paper.

The Bhinjwar is a Dravidian tribe who mainly live in Raipur and Bilaspur district. It is considered to be an offshoot of Baiga of Mandla and Balaghat District of M.P., who occupy the Satpura and Maikal Hills to the north of Chhattisgarh plain. According to Hiralal & Russel (1916) Bhnjhwars are divided into four groups namely (1) Bade Bhinjhwar (2) Sonjhara (3) Binjhia (4) Birjhia. Now a days Birjhia sub group is not found. Binjhia say that they are not at all related to Bhinjhwar.

The Present study is limited to Bade Bhinjhwars only.

Material and Method

The material consists of 233 unrelated Bhinjhwars who were tested both for ABO blood groups and ABH secretion in Saliva. The data were collected from 12 different villages of Raipur District.

The blood was obtained by finger pricking and collected into small test tubes containing citrated Saline. The blood grouping was done on the spot after changing the supernatant saline and plasma for fresh saline two or three times before

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using the cells. The sera were checked daily against the persons of known groups A,B & O.

For collecting Saliva a cotton swab was put into the mouth of the individual and after being soaked with Saliva the subject had to squeeze the liquid into the test tube. Tha Saliva inhibition tests were performed according to the technique outlined by Büchi (1953).

Anti-A, Anti-B and Anti-H Sera used were supplied by the Haffkine Institute, Bombay.

Gene frequencies were estimated according to Bernstein's improved formulae.

Results and Discussion

ABO Blood Groups

The observed and expected frequencies as presented in Table 1 show that the Bhinjhwar is characterised by higher incidences of A and O with low of B. The difference between the observed and expected numbers is not significant (χ^2_1 = .0044. P lies between 0.90 and 0.95).

The gene frequencies are shown in Table 2. The frequencies of the genes "P" and "r" are considerably high, while that of "q" gene is quite low. The D/δ is 0.52, which is less than 2, indicating that the population is in genetic equilibrium as regards to ABO blood group genes.

ABH Secretion in Saliva

The phenotype and gene frequency for the Secretor factor are shown in Table 3. The frequency of Secretor gene (Se= 72.10) is found to be higher than the non-Secretor gene (27.10).

Discussion

In Table 4, the Phenotype and Gene frequencies of some populations residing in Chhattisgarh region and their results have been compared with the Bade Bhinjhwars for the ABO blood groups. Bade Bhatra, Bade & Manjhela Bhatra and the

Bade Bhinjhwar show the highest frequency of blood group A, while Hill Maria, Bison Horn Maria & San Bhatra exhibit the highest frequency of blood group O. In case of Kanwar, All Muria, W. Muria, East Muria, Gond, Manjhela Bhatra, the frequency of blood group B has been found more. It seems that Bade Bhatra, Bade & Manjhela Bhatra, are quite close to Bade Binjhwar in relation to ABO blood group frequency. As they are geographically closer to Bhinjhwar, the intermixture of these groups can not be discarded. On the contrary, Murias & Marias are far off geographically from the Bade Bhinjhwars. According to Naik ('64) and Hiralal & Russel ('16) Bhinjhwars are the offshoot of Baiga. The study of Blood groups of Baiga may throw some light on the genetic relationship between the two tribes.

It is seen that the distribution of gene 'P'is higher among the Bade Bhinjhwar, Bade Bhatra, Bade and Manjhela Bhatra combined in the tribal Population of Chhattisgarh show highest frequencies of 'r' gene as compared to the frequencies of 'p' and 'q' genes.

The frequency of the non-secretor gene se (0.5282) is found to be higher than the secretor gene Se (0.4718) Excepting Mahra, Dorla & Dhurwa, other Tribal groups of Chhattisgarh show higher frequency of the Non-Secretor gene as evident from Table 5.

Summary

ABO blood group and secretor factor of 233 Bade Bhinjhwars have been presented along with their gene frequencies. In ABO blood groups Bade Bhinjhwar are characterised by high incidence of 'A' and 'O' with Low value O, 'B' group. The frequency of Secretor gene (Se. = 72.10) is fairly high than the non-secretor (Se = 27.10) gene.

It is hoped that many more data will be collected from the diverse tribal groups in Chhattisgarh not only with the point of view of ABO Blood group but also of other genetical traits to help in understanding the complex intertribal genetic relationship present in Chhattisgarh.

TABLE 1

Observed and Expected Phenotypes Among the Bade Binjhwars

Total Tested	Observed				Expected				χ^2
	O	A	B	AB	O	A	B	AB	
233	77 (33.04)	83 (35.62)	57 (24.46)	16 (6.87)	76.66 (33.03)	82.65 (33.64)	56.77 (22.64)	15.91 (8.28)	.00441

The figures in parenthesis indicate the percentage.

TABLE 2

ABO Blood Group Gene Frequencies Among the Binjhwars

Unadjusted			Adjusted			D	σ	D/σ
P	q	r	P′	q′	r′			
0.2418	0.1714	0.5748	0.2433	0.1724	0.5843	0.0120	0.0023	0.52

TABLE 3

Phenotype and Gene Frequencies for Secretor Factor

Total Tested	Secretor	Non-Secretor	Se	Se
233	168 (72.10)	65 (27.90)	0.4718	0.5282

TABLE 4

Comparison of the Bade Binjhwars with Other Populations from Chhattisgarh

	Population	Investigator	Total Tested	O	A	B	AB	P	q	r	χ^2 d.f.=1	Probability	Inference
1.	Bade Bhatra	Negi and Ahmed 1963	153	26.14	33.99	29.41	10.46	.2558	.2256	.5185	0.271	.70P.50	Not Significant
2.	Manjhela Bhatra		64	29.69	29 69	34.37	6.25	.2022	.2324	.5653	1.0998	.30P.20	,,
3.	Bade and Manjhela Bhatra		217	27.19	32.72	30.87	9.22	.2379	.2274	.5345	1.998	.20P.10	,,
4.	San Bhatra		88	40.91	18.18	31.82	9.09	.1458	.2292	.6249	1.152	.30P.20	,,
5.	All Bhatra		305	31.15	28.52	31.15	9.18	.2111	.2279	.5609	0.103	.80P.70	,,
6.	E. Muria		143	27.97	25.18	39.86	6.99	.1785	.2742	.5471	1.9090	.20P.10	,,
7.	W. Muria		169	28.99	17.75	38.47	14.79	.1758	.3111	.5131	4.063	.50P.02	Significant
8.	All Muria		312	28.53	21.15	39.10	11.22	.1770	.2941	.5288	0.333	.90P.80	Not-significant
9.	Mahra		123	21.95	30.08	33.33	14.64	.2859	.2781	.4658	0.015	.90P.80	,,
10.	Hill Maria		85	45.9	10.9	34.1	9.4	.1039	.2446	.6515	4.667	.05P.02	Significant
11.	Bisan harn Maria		218	39.0	22.9	29.8	8.3	.1698	.2122	.6180	.509	.50P.30	Not-significant
12.	Gond		129	28.7	26.4	34.1	8.0	.2075	.2579	.5346	0.005	.98P.95	,,
13.	Kanwar		91	17.6	26.4	45.0	10.0	.2122	.3429	.4449	1.502	.30P.20	,,
14.	Bade Binjhwar		233	33.04	35.62	24.46	6.87	'2418	.1714	.5748	.00441	.95P.90	,,

TABLE 5

Comparison of the Bade Binjhwars with Other Populations from Chhattisgarh

Sl. No.	Population	Se	se	Investigator
1.	Bade Bhatra	0.4059	0.5941	Negi and Ahmed
2.	Manjhela Bhatra	0.3876	0.6124	,, ,,
3.	Bade and Manjhela Bhatra	0.4005	0.5995	,, ,,
4.	San Bhatra	0.4161	0.5839	,, ,,
5.	All Bhatra	0.4049	0.5951	,, ,,
6.	E. Muria	0.3310	0.6690	,, ,,
7.	W. Muria	0.4391	0.5909	,, ,,
8.	All Muria	0.3721	0.6279	,, ,,
9.	Mahra	0.5061	0.4939	,, ,,
10.	Dorla	0.5240	0.4796	,, ,,
11.	Dhurwa	0.5050	0.4950	,, ,,
12.	Northern Dhurwa	0.5719	0.4281	,, ,,
13.	Bade Binjhwar	0.4718	0.5282	Present study

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INHERITANCE OF MENTAL DEFECTS AND NEUROMUSCULAR DISORDERS – A CASE OF PLEIOTROPISM

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Inheritance of mental defects and neuromuscular disorders other than those which are demonstrable in terms of chromosomal aberrations and biochemical abnormalities is a complex subject so that any classification of these defects is impossible. However, attempts have been made by various workers (Penrose 1969) to classify them broadly into defects with clinical symptoms and without clinical symptoms. In each of these categories there is such a lot overlapping of symptoms that any further classification is difficult. It is now getting clearer that mental defects are a highly graded character so that any distinct line between feeble mindedness and normality is almost impossible except that one may explain various grades in terms of different levels of I. Q. Similarly distinction between different grades of neuromuscular disorders is also quite difficult. However, distinction between extreme cases is comparatively easier. The subject assumes a greater complexity when one finds a familial history of association and interchanging manifestation of mental defects, defects of the nervous system and muscular system as if in a case of pleiotropism. In the present paper a large pedigree has been analysed to throw additional light on the wide range of variability that exists in this pleiotropic character and explain the mode of heredity and possible role of environment in the manifestation of these disorders.

Material and Method

The material for this paper consists of a large pedigree consisting of 69 members in which occurrence of mental defects including mental derangement epilepsy, subnormal intelligence and other neuromuscular disorders have been traced through

four generations. As far as possible the author interviewed all the living members of the pedigree and even some of those who are now dead. Information about the mental status of those who were confined to mental asylum was obtained from records of mental asylum, while for others it was done with the help of competent psychologists, and also on the basis of their performance at school and in job. Clinical histories of the patients with neurological and muscular disorders were available from relatives and hospital records and are presented below:

Case History of the Afflicted Persons in the Pedigree

I_2. He suffered from epileptic fits accompanied by twitching of muscles since adolescence. Died at the age of 40 years due to fall in a well, either accidentally or an attempt to commit suicide. No information regarding his mental status is available. His relatives reported that otherwise he was physically and mentally normal.

II_2. He was born normal. Dull at studies and could not pass Matriculation examination despite repeated efforts. Helped his father in business. After his father's death entered into a partnership with some body else and continued in business till the age of 40 years. In the meantime his partner deceived him so that he suffered from a severe mental shock from which he never recovered. He was forced to give up business and take up a petty job in an office. His mental condition continued deteriorating. He suffered from a sense of economic insecurity and social neglect. Blamed everybody around him especially his well-to-do relatives. Showed signs of abusive and violent behaviour. Left the job and was admitted to a lunatic asylum. Showed some signs of improvement after an year or so. He was then discharged from the asylum. Again after a few months showed signs of mental derangement and continued in the same state with occasional short remissions till he died at the age of 60 years. All clinical examinations produced negative results.

III_{10}. He was born normal. Dull at school, could not pass Matriculation despite repeated efforts. Held a petty job in an office. He showed signs of mental derangement at the age of 35 years but managed to stick on to the job for about 20 years

but without receiving any promotion. Aggressive and violent in behaviour. Talks too much. Suffers from hellucinations and meglomania. People dismiss him as a mad cap. His financial condition is sound since he has inherited a good fortune. Living at the age of about 70 years.

III_2. He was born normal. He is of normal intelligence, did well at school and college and well settled in life. At the age of 30 years, showed signs of neuromuscular disease and was diagnosed as suffering from lack of coordination between nerves and muscles. Living at the age of 40 years.

III_3. She was born normal. She was of normal intelligence through out. Got married at the age of 20 years. Showed signs of insanity first at the age of 25 years. Ever since then she had been showng occasional fits of insanity. In such a state she gets excited, talks out of context and accuses people around her. Living at the age of 38 years.

III_6. She was born normal. At the age of ten years she had her first epileptic fit. Frequent fits continued through out adolescence and even after she got married at the age of 19 years. During epileptic fits she used to experience twitching of muscles, threw out the tongue and bit it hard every time. Electroencephalographic examinations showed dysrhythmic cerebral activity. She had very weak memory. Died at the age of 25 years.

III_7. He was born normal. During his childhood showed signs of weak memory, acute stammering and lack of interest in studies. Could not study beyond primary class. Showed distinct signs of insanity at adolescence and indulged in abusive and violent activities. He was then admitted to lunatic asylum. Ran away from there after a few months. Loiters about in the street, once roped in by criminals to help them commit theft in his own house. Living at the age of 30 years. Clinical tests failed to reveal the pathology.

III_8. He was born normal. Through out he has been weak at studies, could not do beyond primary education. He shows low I.Q. (70–80). Living at the age of 25 years.

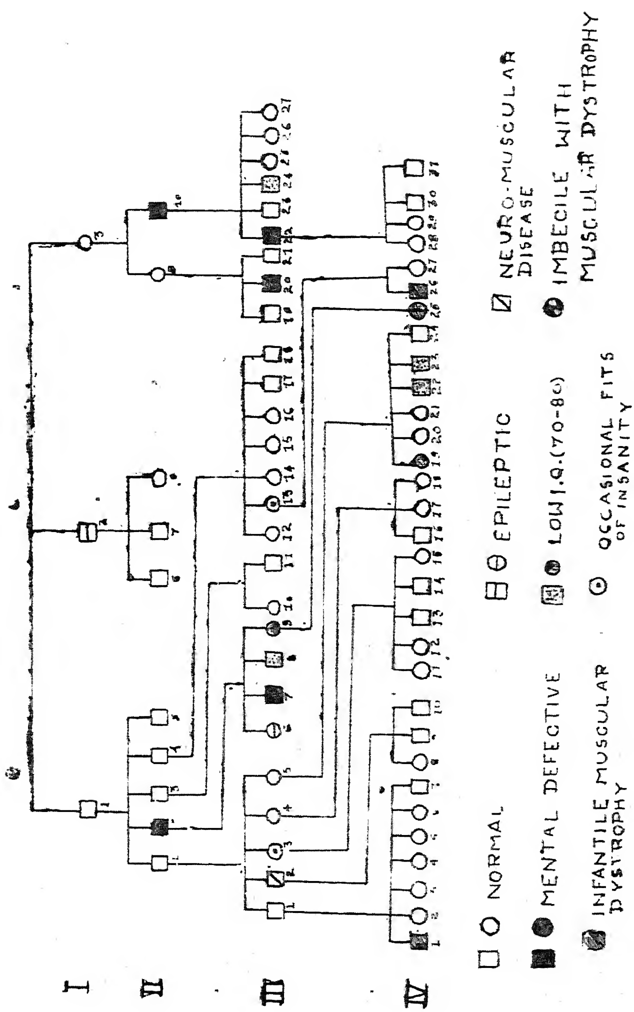
I
II
III
IV
NORMAL
MENTAL DEFECTIVE
INFANTILE MUSCULAR DYSTROPHY
EPILEPTIC
LOW I.Q.(70-80)
OCCASIONAL FITS OF INSANITY
NEURO-MUSCULAR DISEASE
IMBECILE WITH MUSCULAR DYSTROPHY

Figure 1

III_9. She was born normal. She was weak at studies with stammering speech and low I.Q. (about 80) through out childhood and adolescence. She got married at the age of 20 years. Died after an year or so during child birth.

III_{18}. She was born normal, showed normal intelligence through out childhood and adolescence. Got married at the age of 20 years. She got a son who was later at the age of four years diagnosed as suffering from muscular dystrophy. When she learnt that her son was suffering from an incurable disease, she started having fits of insanity intermittently and behaves abnormally when she is in a state of mental derangement. Living at the age of 28 years.

III_{20} He was born normal. Insane since childhood. As he grew up indulged in violent acts and therefore remained chained and locked up in a room at home till he died at the age of 30 years. No clinical history was available.

III_{22}. He was born normal. Insane in childhood. Never could study. At the age of 20 years admitted to lunatic asylum. Discharged after about an year without any improvement in the condition. Showed no clinical symptoms. Not very violent in action but uses violent and abusive language. His relatives managed to get him married fraudulently at an early age thinking he might improve but with no positive results. His wife works and looks after him. Living at the age of 42 years.

III_{24}. He was born normal. He has low I.Q. (80). Living at the age of 23 years.

IV_1. He was born normal, but suffered from infantile progressive muscular dystrophy at the age of two years. Died at the age of three and half years.

IV_{18-20}. They were born normal. Weak in studies through out and could not pass at school even after repeated efforts. Psychological examinations showed low I.Q. (70–80), stammering speech, living at the ages of 28, 23 and 21 respectively.

IV_{25}. He was born normal. At the age of four years showed signs of infantile muscular dystrophy. Living at the age of seven years though extremely lean and thin, with retarded bony and muscular growth.

DISCUSSION

In the present pedigree (Fig. 1) the frequency of epilepsy (3.0%), mental derangement (7.0%), neuromuscular disorder (4.0%), and subintelligence (8.5%) is considerably higher than in the general population, indicating a definite familial basis for the diseases. However, definite clinical tests for Pathology of mental derangement have failed to produce any positive results. In the case of epileptics, neuromuscular disorders and subintelligence the medical reports and psychologist's reports have been quite revealing. All the diseases manifest in the pedigree under discussion although may be broadly classified as diseases of the nervous system but on the basis of preponderance it is possible to say that disease of the nervous system in some measures is primary to muscular diseases. The question of importance therefore arise whether or not all these defects are manifestations of the same genetic factors and whether some of them could be attributed to interaction of genetic and environmental factors also. In the pedigree there are evidences for both the possibilities which appear to be acting in a rather complimentary manner.

There are many reports in the literature which deal with high familial incidence of epilepsy, mental derangement and neuromuscular disorders (Sanders, 1933; Rosanoff, Handy & Rosenoff, 1934; Penrose, 1938, 1969; Allen and Kallman, 1962; Reed and Reed, 1965). Brown (1930) investigated the relatives of epileptic patients and found 64% of the patients had epileptic relatives and 89% had relatives who were either epileptic, insane or mentally deficient, 78% had psychosis and 25% mentally defective relatives. Almost similar picture is obtained in the present investigation where mentally deranged father has given birth to mentally deranged son, epileptic daughter and two other children, a daughter and a son, with low I. Q. Similarly persons with neuromuscular disease had relatives who were epileptic, mentally deranged and mentally deficient.

It is interesting to note in the pedigree that normal brother and sister of the epileptic patient (12) have given birth to mentally deranged sons, while the epileptic himself has given birth to normal children. Again these mentally deranged sons have given birth to mentally deranged sons, dullards with low I. Q.,

epileptic as well as normal children. It seems likely therefore, that the same gene or set of genes is responsible for all these related defects while their variable expression might depend upon the extent of penetrance of the genetic factors or may be due to the allels that partner the genes. This fact is amply demonstrated by the pedigree where members show graded manifestation of the severity of both mental derangement and neuromuscular disorders. Sex seems to play an influencing role in the expressivity of the traits so that males have been found to be effected more frequently and more severely than females. Two of the females (III3 & III 13) who seem to have inherited the mental defect, show only occasional fits of insanity. Also, mentally deranged males in the present pedigree who have often shown a violent or near criminal disposition are typologically quite distinct from idiots or imbeciles. Allen, Herndon and Dudley (1944) reported a pedigree in which conditions like imbecility associated with pseudohypertrophic muscular dystrophy and in some cases neurological symptoms were inherited as a sex linked character and was confined to males and transmitted through normal females through five generations. In the present pedigree there are evidences that the genetic factors for the diseases are carried on the autosomal chromosome and behave as recessive and dominant recurrently. That this dual behaviour could be due to certain environmental factors – psychological or socio-economic, which may have triggered the onset of the disease in some individuals which otherwise may have passed down as recessive, is suggested by the personal history of at least two of the individuals (II2 & III 13) in the pedigree.

Acknowledgements

The author is thankful to the members of the pedigree who allowed themselves to be investigated and for providing useful information including clinical and psychological reports.

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A STUDY ON THE DERMATOGLYPHIC PATTERNS IN MONGOLS

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INTRODUCTION

The dermatoglyphic Patterns of mongols are characterised by the presence of transverse palmar crease, a single crease on the fifth finger, a triradius near to the centre of the Palm, absence of pattern on the thenar eminence and a tendency for loops to occur on every finger rather than whorls or arches (Baikie, 1965). Walker (1957) has compared the dermatoglyphic pattern of mongols with that of the normal persons and Smith (1966) has noted an approximate figure for the normal dermatoglyphic patterns and the patterns in mongols.

Maternal age has a greater influence on the type of mongols. Usually younger mothers give birth to translocation mongols where as elderly mothers give birth to trisomy ones. In case of translocation mongols there is further chance of getting more mongols in the blood relations. As translocation mongols are commonly born to younger mothers it was intended to find out if there is any variation in the Palmar dermatoglyphic Patterns of mongols born to younger and elderly mothers.

MATERIALS & METHODS

Sixteen cases diagnosed clinically as mongols were studied. The first group includes those whose mothers were less than twenty-five years of age at the time of their birth and the second group includes those whose mothers were more than thirty years of age. The dermatoglyphics were studied by direct visual technique and included the digital, interdigital, thenar, hypothenar and hallucal Patterns, the position of the axial triradius, the presence of simian crease and the third interdigital crease on the little fingers.

Observations

From Table 1 it could be concluded that ulnar loops are more common in the digits and they are equal in both groups. Whorls were more in Group I and arches were more in Group II. In Group I the ulnar loops were almost equal in both the Palms where as in Group II ulnar loops were more common in the right than the left.

TABLE 1

Represents the Digital Patterns in Both Groups, Expressed in Terms of Percentages

Digital Patterns	Group I										Total	Group II										Total
	1		2		3		4		5			1		2		3		4		5		
	L	R	L	R	L	R	L	R	L	R		L	R	L	R	L	R	L	R	L	R	
Lu	86	100	100	100	86	86	43	43	71	71	79	100	89	67	89	67	89	56	78	67	89	79
Lr	–	–	–	–	–	–	14	–	–	–	1	–	–	–	11	–	–	11	–	–	–	2
W	–	–	–	–	14	14	43	57	29	14	18	–	11	22	–	22	11	22	11	33	–	13
A	14	–	–	–	–	–	–	–	–	14	3	–	–	11	–	11	–	11	11	–	11	6

Table 2 shows that $1D_3$ and $1D_4$ Patterns, Simian crease and distal axial triradius are more common in Group II. Hallucal arch tibial Pattern is present in 100% cases of Group II where as it is present in 64% of cases of Group I. Changes in the fifth finger is marked in 66% of cases in Group II but only in 57% of cases in Group I. However, a single crease on the fifth finger is present in 33% of cases in Group II, whereas it is not seen in any case of Group I.

TABLE 2

Represents the Patterns in Palmar and Plantar Areas in Both Groups. Expressed in Terms of Percentages

Palmar and Plantar areas	Group I			Group II		
	Left	Right	Total	Left	Right	Total
$1D_1$	0	0	0	0	0	0
$1D_2$	29	0	14.5	11	0	5.5
$1D_3$	85 (Arch & Loop)	85 (Arch & Loop)	85	89 (Arch & Loop)	89 (Arch & Loop)	89
$1D_4$	29	29	29	44	56	50
Thenar	0	0	0	0	11	5.5
Hypothenar	29	29	29	11	22	16.5
Simian	57	43	50	56	67	61
Triradius	86	86	86	89	89	89
Single crease on 5th finger	0	0	0	33	33	33

Rudimentary 2nd Phalanx on 5th finger	57	57	57	33	33	33
Hallucal (A.T.P.)	71	57	64	100	100	100

The important findings in Tables 1 and 2 are summarised in Table 3 and compared with the normal figures as quoted from Smith (loc cit.). It could be concluded that the Palmar and hallucal Patterns as suggested to be typical of mongols are more frequent in those born to elderly mothers.

TABLE 3

	Mean Percentage of digits having ulnar loops	Frequency of distal axial triradius	Hypothenar Pattern	$1D_3$ Pattern	Simian crease	Single crease on 5th finger	Hallucal Patterns
Normal	64%	7%	—	—	4.9%	—	Rare
Group I	79%	86%	29%	85%	50%	0%	64%
Group II	79%	89%	16.5%	89%	61%	35%	100%

According to Dent et al (1963), translocation mongols might be relatively mildly affected. In other words the signs are less manifest in translocation mongols than in the trisomy ones. As translocation mongols are commonly born to younger mothers the present study suggests that the dermatoglyphic patterns are also less pronounced in translocation mongols than the trisomy ones who are usually born to mothers at an advanced age. However, it is necessary to confirm this by chromosome studies.

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DOWN'S SYNDROME IN COASTAL ANDHRA PRADESH

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INTRODUCTION

Over a hundred years ago, Langdon Down (1866) described the facial features and other characteristics of a group of patients who appeared to him to have some physical similarity among themselves and with Mongolian people. A significant development came in 1959, when Lejeune, Gautier and Turpin described the occurrence of an additional small acrocentric 'G' (21–22) group chromosome as the basic defect in mongoloid patients. Cytogenetical testing for this extra chromosome has now become routine in establishing the diagnosis of Down's Syndrome or mongolism, which is also referred to as trisomy 21. Soon after the discovery of trisomy 21 in Down's Syndrome, Polani et al (1960) reported a female case with Down's Syndrome, which showed forty-six chromosomes in her bone marrow cells. There were four small acrocentric chromosomes as in a normal female, five medium sized acrocentric (Nos. 13–15) and an extra submedian chromosome of the size similar to group C (Nos. 6–12, X) chromosomes. Karyotype analysis showed that reciprocal translocation involving a chromosome 21 and possibly a chromosome 14 (Denver classification) had most probably occurred.

However, according to the recent development of chromosome study, Down's Syndrome is known to involve a typical Karyotype besides the above described two typical Karyotypes (Table 1).

MATERIAL AND METHOD

Most of the cases were collected from King George Hospital, Visakhapatnam. Two cases were collected from the

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Rani Chandramati Devi Hospital for handicapped children which is a rehabilitation centre affiliated to the paediatrics department of King George Hospital, Visakhapatnam.

Chromosome analysis was carried out on blood cells by the method of Moorhead et al (1960) with slight modifications. In general eleven metaphase were analysed in every sample. The chromosomes were described using the Denver nomenclature.

TABLE 1

An Appraisal of the Chromosomal Aberrations of Down's Syndrome

Name of the authors first described	Chromosome number	Conclusions
Lejeune et al (1959)	47	trisomy 21
Polani et al (1960)	46	translocation 13/21
Carter et al (1960)	46	translocation 14 or 15/21
Fraccaro et al (1960)	46	reciprocal translocation between two of the triplicated No. 21
Penrose et al (1960)	46	reciprocal translocation between No. 21 and No. 22.
Fitzgerald et al (1961)	46 47 48	normal trisomy 21 tetrasomy 21 } Mosaicism
Gustavson et al (1961)	46 47 48	normal trisomy 21 trisomy 21 & isochromosome } Mosaicism
Hammerton et al (1961)	46 47	isochromosome for the long arm and of two No. 21s and a No. 21 isochromosome for the long arm of two No. 21s and two No. 21s } Mosaicism
Gray et al (1962)	46	pericentric inversion of a prenatal No. 21.
Tsuboi, Inouye (1962)	47	isochromosome for the long arm of two No. 21s of the quadruplicated No. 21.

Discussion

In the present series, nine mothers were in the age groups between 20 and 25 years, constituting 75% of the total sample studied, while the remaining cases were between 30 and 40 years (Table 2). The age distribution presented a bimodal picture, because of two categories of age groups.

Seventy-five per cent of the fathers were in the age groups 24 to 30 years while the rest 25% of them were in the age group between 40 and 45 years (Table 2). A study in this direction does not prove to be of any value, as stated by Penrose (1962), that there is no definite correlation between paternal age and chromosomal nondisjunction.

Table 2

Parental Age, Marriage Type and the Order of Birth in the Present Series

Case number	Maternal age at the birth of the patient	Paternal age at the birth of the patient	Marriage type	Order of birth
1	20	25	affinal	II
2	20	24	consanguineous	I
3	21	27	,,	III
4	22	28	,,	I
5	20	30	affinal	I
6	21	27	,,	I
7	23	26	,,	I
8	24	28	consanguineous	III
9	21	26	affinal	I
10	30	40	consanguineous	III
11	40	45	affinal	X
12	36	45	,,	V

In contrast to the statement (Penrose 1939) that a Mongol is the last one of a large family, fifty per cent of our cases were the first born. Of the remaining six cases, one (8.3%) was the second born, three (25%) were third born, fifth and tenth respectively (Table 2).

The incidence of consanguineous marriages of the parents was 41.3% in the present series (Table 2). Since the abnormality in Down's Syndrome is apparently not a gene determined factor this high incidence of consanguineous marriage probably has no etiological significance. The fact remains that the incidence of consanguineous marriage is particularly high in coastal Andhra Pradesh (Chakravartti, et al 1971), explains the reason why the data from contemporary series do not show such high figures.

The oblique upward and outward slant of the palpebral fissure was present in 66.6.% of the cases in the present series (Table 3). The same finding was given diagnostic significance for the "Mongoloid" slant of the eye (Figure 1).

Increased space between the first and second toes was present in 66.6% of the cases examined, and this is occasionally seen in normal individuals (Table 3, Figure 2).

TABLE 3

Clinical and Cytogenetic Findings in the Present Series

Case number	Epicanthic fold	Single Simian crease	Space between I and II toes	Chromosomal findings
1	present	single crease	wide	G-trisomy
2	,,	,,	,,	,,
3	not well marked	,,	,,	,,
4	,,	no single crease	,,	,,
5	present	,,	not wide	,,
6	,,	single crease	wide	,,
7	,,	no single crease	not wide	,,
8	,,	single crease	wide	,,
9	,,	no single crease	not wide	,,
10	not well marked	single crease	,,	,,
11	present	,,	wide	,,
12	not well marked	no single crease	,,	,,

Figure 1
Typical face of Down's syndrome

Figure 2
Feet showing the wide gap between first and second Toes

A single palmar transverse crease was present in both hands in seven children (57.5%) of the observed cases (Table 3, Figure 3). This confirms that they form only a part of the clinical pattern of Down's Syndrome.

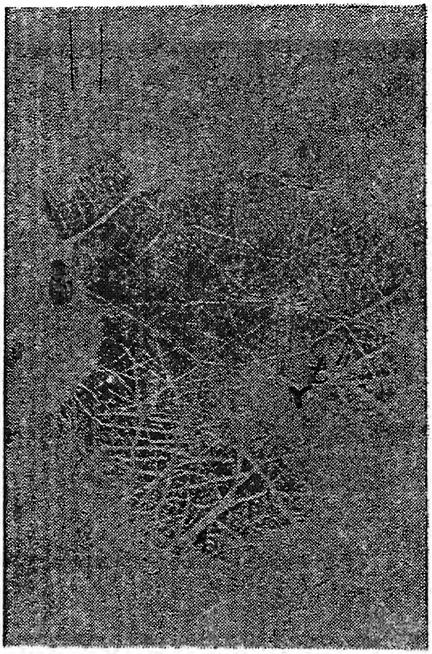

Figure 3 : Palm print showing single Palmar Crease

The cytogenetic study revealed that the trisomy of the 'G' group is the commonest aberration in the present series (Table 3, Figure 4). Translocation and other atypical cell lines were not observed in the present series.

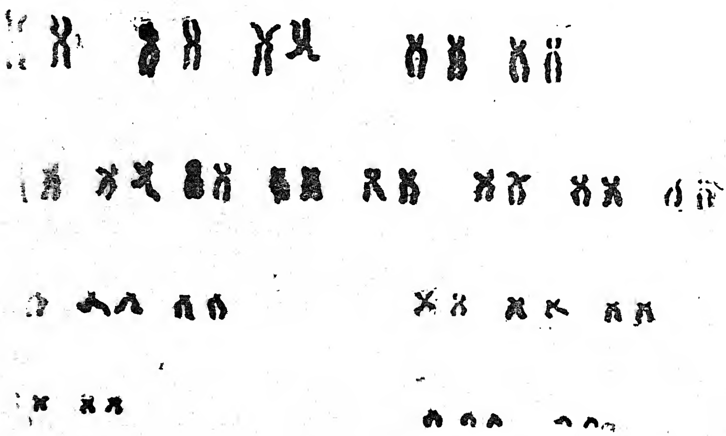

Figure 4 : Metaphase of the Female showing 'G' Trisomy

Summary

A detailed study of the various aspects of Down's Syndrome was carried out with practical application of cytogenetics.

Though the present series comprises only 12 cases, in the light of certain observations the material is considered to be of immense genetical significance. Many of the findings are in concordance with the earlier reports while many a discordant views are also recorded for further confirmation.

Acknowledgement

The author is grateful to Dr. M.R. Chakravartti, Reader in Physical Anthropology, Andhra University, Waltair (A.P.) for his valuable guidance in preparing this paper.

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KLINE-FELTER'S SYNDROME

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In 1942 Kline-felters, described a syndrome in post puberal males consisting of small testes with Tubular Hyalinisation, azoosperma, gynaecomastia and low concentrations of urinary 17-Ketosteroids. Several years later Bradbury et al (1956) and Plunkett and Barr (1956) noted chromatin Positive nuclei with 47/XXY chromosomal complement. Since then all patients reported with bilateral testicular dysgenesis and primary micro-orchidism with sex-chromatin positive nuclei have had 47/XXY sex-chromosome constitution or of its variants.

New born males with Klinefelter's do not exhibit any remarkable symptoms and the condition is usually not detected until puberty or later at infertility clinics or mental Asylums with mental retardation. Other clinical findings are sparse-facial and abdominal hair, enuchoidism, small phallus. Gynaecomastia has been invariably seen in our patients though in the literature, 40% of XXY males show this feature.

The majority of the males with this syndrome have a 47/XXY chromosome complement, other variants like 46/XY/47/XXY; 48/XXXY, and 49/XXXXY chromosome complements have been described.

The incidence of sex chromatin positive males is greater in mental Institutions (10 per 1,000), than in the newborn population (2.06 per 1,000) (Maclean et al 1964). Thus it appears that the degree of mental retardation and testicular lesion is enhanced with an increase in the number of X chromosomes.

Case Report

A.S. 20 years male admitted with Gynaecomastia and Infantile genitalia for detailed investigation and diagnosis and for removal of breasts.

Family History: Two brothers and two sisters. No similar complaint in the family members and no consanguinity of marriage of his parents. He is the third in the family of four.

General Examination: Moderate height of 5′ 2″, with Bilateral Gynaecomastia and Primary small fibrosed testes in the scrotum, small penile structure.

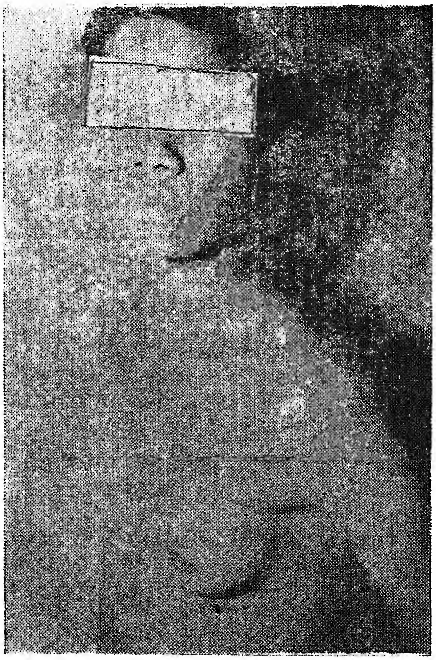

Figure 1

Photograph of K. F. Syndrome showing Bilateral Breasts and male Phenotype

Investigations: Hb: 10 gms%. Blood smear showed 30% of Drumsticks single mostly with occasional double drumsticks; Buccal mucosal cells showed 35% Barr bodies. TW BC: 7500 cells/cmm. 17—Keto steroids in urine: 4.5 mgm/24 HRS urine.

Chromosome Analysis: Showed 47/XXY Chromosome complement as done by (T.C. 199 medium culture Micromethod)

Testicular Biopsy: Showed sclerosed Tubules with Interstitial leydig cell Islands. Some of the Tubules showed sertoli cells only. No evidence of spermatogenesis.

Discussion

A case of typical Klinefelter's syndrome characterised by small testes with Azoospermia gynaecomastia and chromatin positive male who showed a 47/XXY chromosome complement was described in this paper.

This condition is not detected until they reach puberty or later at Infertility clinics for sterility.

The gonads, the testes of these individuals are deficient in spermatogenesis and the tubules show sclerosis or living with sertoli cells only. The leydig cells are in clumps and immature.

The majority of these cases shows 47/XXY chromosome complement and sex-chromatin will be positive in Buccal mucosal cell screening. Two other frequently observed Karyotypes from individuals with K.F. syndrome cases are 46, XY/47, XXY mosaics and 48, XXXY (New et al 1972). In the former microorchia is found in only 78%, Azoospermia in 57%, and 32% had subnormal intelligence. 30% of these mosaic men are believed to have fathered offspring so the presence of the normal XY cell line apparently diminishes the effect of 47/XXY cell line. The men in the latter group 48, XXYY were found the clinically similar to XXY individuals but taller, Eunuchoid and more retarded (Schlegal 1965).

Summary

1. A case of Typical Klinefelter's syndrome with gynaecomastia bilaterally and primary microorchidism is presented.

2. His Karyotype analysis showed 47, XXY chromosomal complement with sex-chromatin positive in Buccal mucosal cells screening.

3. Other chromosomal patterns and pathogenesis of K.F. Syndrome discussed.

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INBREEDING IN COASTAL ANDHRA PRADESH

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It is interesting to note that Andhra Pradesh with its high rate of inbreeding forms a rich fertile field for studying the inbreeding rate and the biological effects of inbreeding in populations, which are valuable, in a practical way, for genetic counselling. Very few data have so far appeared in literature on inbreeding in various population groups of Andhra Pradesh.

MATERIALS AND METHODOLOGY

The present paper reports the incidence of inbreeding in three caste groups namely Kammas, Salis, Jalaries and among two tribal populations by name Koyadora and Kondareddi of East Godavari and Visakhapatnam Districts of Coastal Andhra Pradesh. This investigation is a follow up study of our survey of consanguinity on the incidence among Kapu caste in Coastal Andhra Pradesh undertaken during 1969–70. The survey covered two villages by name Draksharama, (Sali caste) Panangipalli (Kamma caste) in East Godavari District, a group of nine villages Rampachodavaram block of East Godavari District (Koyadora and Kondareddi tribes) and Jalaripeta (Jalari caste) in Visakhapatnam District. The various samples of consanguineous marriages recorded in various groups are as follows. Kammas – 62; Salis – 82; Koyadora – 154; Kondareddi – 137 and Jalaries – 102. These data have been pooled together with the previous data of Kapu caste collected from the different villages of East Godavari and Visakhapatnam Districts and presented here.

The present data has been subjected to different comparative analyses. The data has been analysed district-wise, caste-wise and tribe-wise. The rates of inbreeding and the values of inbreeding coefficient for autosomal genes and for sex-linked genes have also been calculated, (F and F_1), this excess for sex-linked

genes being contributed entirely by the matrilateral cross-cousin marriages. A comparison has been attempted between the castes and tribes of two districts of C.A.P. including inter and intragroup variations.

RESULTS

Geographical Variation

The data analysed according to districts (Table 1) show that the highest concentration inbreeding (48.5%) is seen in Visakhapatnam District ($F=0.038$ and $F_1=0.054$) than in East Godavari District ($F=0.033$ and $F_1=0.041$). The inbreeding rate also diminishes in East Godavari District (35.7%). The data pooled together from the two districts presents a total consanguineous rate of 39.1%, the values of F and F_1 being 0.035 and 0.044 respectively. Among castes of Visakhapatnam district, in Jalaries the consanguinity is more vigorously practised (47.06%) while in East Godavari, among Kammas, one of the the predominant castes of A.P. it is highly practised (43.3%).

Social Variation

Table 2 shows the data analysed according to castes in two districts combined together. The highest rate of inbreeding is practised in Jalaries (47.06%) with the values of F and F_1 being 0.038 and 0.054 respectively. Next to that seen in Kammas with a rate of 43.3%. The F and F_1 values represent 0.042 and 0.046 respectively, while the Kapus and Salis show low levels of inbreeding (34.05% and 27.28% respectively) with the values of F and F_1 for Kapus being 0.025 and 0.034 and for Salis being 0.02 and 0.031 respectively. The data pooled together from all castes present a rate of 35.36% with the values of F and F_1 being 0.031 and 0.041 respectively.

Further the data available on tribes and castes from the two districts are compared with each other (Table 3). It is seen that a higher rate of inbreeding (51.5%) is reported in tribal populations ($F=0.044$ and F_1 0.052) than in castes ($F=0.031$ and F_1 0.041). The inbreeding rate also diminishes in caste populations (35.36%).

TABLE 1

District-wise Data (Rate of Inbreeding and F and F_1 Values)

District	Village	Caste or Tribe	No. of Marriages	Consanguineous marriages 1 C Mat. cr. cou.	1 C Pat. cr. cou.	UN	ICI	2C	F	F_2	Total No. of Con. marriages and rate of Consanguinity	
Visakha-patnam	Golazam	Kapu (ca)	230	55	29	29	—	—	0.038	0.053	113	(49.13%)
	Vadapalem	Jalari (ca)	102	26	8	14	—	—	0.038	0.054	48	(47.06%)
	Total		332	81	37	43	—	—	0.038	0.054	161	(48. 5%)
East Godavari	Kapavaram and Vella	Kapu (ca)	510	57	22	33	3	24	0.017	0.023	139	(27.28%)
	Panangipalli	Kamma (ca)	60	4	1	17	3	1	0.042	0.046	26	(43. 3%)
	Draksharama	Sali (ca)	82	15	3	4	—	—	0.020	0.031	22	(26. 8%)
	Rampa-chodavaram	Koyadora (tr)	154	18	25	36	—	—	0.047	0.054	79	(51. 3%)
	Rampa-chodavaram	Kondareddi (tr)	137	23	33	15	—	—	0.040	0.050	71	(51. 8%)
	Total		943	117	84	105	6	25	0.033	0.0411	337	(35. 7%)
	Grand Total (Two Districts)		1275	198	121	148	6	25	0.035	0.044	498	(39. 1%)

Note : Ca – Caste; Tr – Tribe; 1C – First Cousin; 1CI First Cousin once removed; 2C – Second cousin; Mat. cr. cou.– Matrilateral cross-cousin; Pat. cr. cou. - Patrilateral cross-cousin; UN - Uncle-niece.

TABLE 2

Comparison of Inbreeding Rate and F and F_1 Values between the Data of Various Castes in Two Districts Combined Together

Caste group	No. of Marriages	Consanguineous Marriages Mat. cr. cou. (1 C)	Pat. cr. cou. (1 C)	UN	ICI	2C	F	F_2	Total No. of Con. marriages and rate of Consanguinity
Sali	82	15	3	4	—	—	0.020	0.031	22 (26. 8%)
Kapu	740	112	51	62	3	24	0.022	0.031	252 (34.05%)
Kamma	60	4	1	17	3	1	0.042	0.046	26 (43. 3%)
Jalari	102	26	8	14	—	—	0.038	0.054	48 (47.06%)
Total	984	157	63	97	6	25	0.031	0.041	348 (35.36%)

TABLE 3

Comparison of Inbreeding Rate and F and F_1 Values between the Data of Various Castes and Tribes in two Districts Combined Together

Caste or Tribe	No. of Marriages	Consanguineous Marriages Mat. cr. cou. (1C)	Pat. cr. cou. (1C)	UN	ICI	2C	F	F_1	Total No. of Con. marriages and Inbreeding rate
Sali (ca)	82	15	3	4	—	—	0.020	0.031	22 (26. 8%)
Kapu (ca)	740	112	51	62	3	24	0.025	0.034	252 (34.05%)
Kamma (ca)	60	4	1	17	3	1	0.042	0.046	26 (43. 3%)
Jalari (ca)	102	26	8	14	—	—	0.038	0.054	48 (47. 6%)
Total (ca)	984	157	63	97	6	25	0.031	0.041	348 (35.36%)
Koyadora (Tr)	154	18	25	36	—	—	0.047	0 054	79 (51. 3%)
Kondareddi (Tr)	137	23	23	15	—	—	0.040	0.050	71 (51. 8%)
Total (Tr)	291	41	58	51	—	—	0.044	0.052	150 (51. 5%)
Grand Total (ca+Tr)	1275	198	121	148	6	25	0.035	0.044	498 (39. 1%)

An attempt has also been made to account for the most preferred types of consanguineous marriages among the various castes and tribes of two districts of Coastal Andhra Pradesh (Table 4). It is observed that in tribal population the patrilateral cross-cousin (Kondareddi) and uncle niece types (Koyadora) are more frequent ones whereas in caste groups the matrilateral cross-cousin and uncle niece types are mostly preferred. On the whole it is observed that matrilateral cross-cousin type of marriage (15.5%) is more prevalent in these areas, while the uncle niece marriage comes as second preferential type of marriage. Sanghvi's (1966) data agrees to this print while Dronamraju and Meerakhan's (1960–1963) data disagrees, which reports the high incidence of patrilateral cross-cousin type followed by uncle niece type of marriage. So also Chakravartti's data (1968) on Kolam tribe of Adilabad district reports the more prevalence of Matrilateral cross-cousin type of marriages in contrary to the picture presented in the present data of tribes here.

Discussion

For the genetic study of any population it is essential first to understand the social structure and marital custom of its people. The traditional organization of the Hindu Society into various castes and subcastes is still rigid and these groups have remained largely endogamous.

The Hindu caste system of India has probably been the subject of more study and speculation than any other social stratification system in the World (Majumdar, 1961, Kapadia, 1947 and others).

It is clear from the data presented that there has been high rate of inbreeding among the people of Andhra Pradesh. This has been known and socially accepted for many hundreds of years. The socio-economic reasons for the high incidence of consanguineous marriages in India have been outlined by Dronamraju and Meerakhan (1963) Sanghvi (1966) and Chakravartti (1968).

The present survey of inbreeding in rural areas of Coastal Andhra Pradesh is based on a sample of 1275 marriages. The

main feature of the data is a high proportion of matrilateral cross-cousin types and uncle niece types, which accounted almost for one out of every four marriages. The coefficient of inbreeding is 0.035 for autosomal genes and 0.044 for sex linked genes, the excess for sex linked genes being contributed by the matrilateral cross-cousin marriages. These levels of inbreeding, which are perhaps the highest coefficients, so far recorded in any large human population, may be compared with some theoretical values. If, for instance, a population was perpetuated entirely by first-cousin marriages, the coefficient of inbreeding would be 0.0625. If it was continued by marriages only of first-cousin once removed, the cofficient would be 0.0313. The figures for Coastal Andhra Pradesh lie between these theoretical values. The same conclusion could be derived from Sanghvi's data (1965) on Visakhapatnam and East Godavari Districts, the values of F and F_1 being 0.047 and 0.065 respectively. But the data of Dronamraju and Meerakhan (1960 and 1963) disagrees to this point. The values of inbreeding coefficients (F & F_1) were 0.023 and 0.024 respectively in data collected in 1960 and 0.0209 and 0.0239 in data collected in 1963.

An attempt has also been made to compare the present data (Table 5) with the past data available so far from the same area – Dronamraju and Meerakhan (1960 and 1963); Sanghvi (1966). Dronamraju and Meerakhan in their two surveys in 1960 and 1963 recorded about 31% consanguineous marriages in the Coastal Andhra area while Sanghvi data (1966) showed a high concentration of consanguineous marriages (52%).

To quote Sanghvi (1966) "Data analysed according to districts showed that the highest concentration of inbreeding was in the coastal areas of Visakhapatnam and East Godavari and that the concentration gradually diminished in the interior districts". The present data giving a different picture of these two works, reports the rate of inbreeding as 39.1%. This shows that there is a decreasing trend in the practice of consanguineous marriages among the people of Coastal Andhra Pradesh in the present years. Various socio-economic reasons can be attributed to this trend.

TABLE 4

List of Mostly Preferred Type of Consanguineous Marriages Among Various Castes and Tribes

Caste or Tribe	Total No. of Marriages	Consanguinity Rate	Rate of preferred type of inbreeding
Sali (ca)	82	26. 8% (22)	18. 3% (15) Mat. cr. cou.
Kapu (ca)	740	34.05% (252)	15.13% (112) Mat. cr. cou.
Kamma (ca)	60	43. 3% (26)	28. 3% (17) UN
Jalari (ca)	102	47.06% (48)	25. 5% (26) Mat. cr. cou.
Koyadora (Tr)	154	51. 3% (79)	23.37% (36) UN
Kondareddi (Tr)	137	51. 8% (71)	24% (33) Pat. cr. cou.
Total	1275	39. 1% (498)	(15. 5% (198) Mat. cr. cou.; 11. 6% (148) UN)

TABLE 5

Comparison of Inbreeding Rate and F and F_1 Values in the Present Data with the other Data (from Visakhapatnam and East Godavari Districts Combined Together)

Name of the source	No. of Marriages	Consanguineous Marriages Mat. cr. cou. 1C	Pat. cr. cou. 1C	UN	IC1	2C	F	F_1	Total No. of Con. marriages and inbreeding rate	
Dronamraju and Meerakhan (1960)	327	6	48	29	10	9	0.023	0.024	102	(31.19%)
Dronamraju and Meerakhan (1963)	2177	1C 362		157	147		0.0209	0.0239	666	(30. 6%)
Sanghvi (1966) (E.G. and Vizag only)	1249	362	11	277	—	—	0.047	0.065	650	(52%)
Present data (1970) (Pooled together)	1275	198	121	148	6	25	0.035	0.044	498	(39. 1%)

TABLE 6

Comparison of Inbreeding Rate and F and F_1 Values in the Present Tribal Data with the other Data of Tribes (in A.P.)

Tribe	No. of Marriages	Consanguineous Marriages					F	F_1	Total No. Con. marriages and inbreeding rate	
		Mat. cr. cou. 1C	Pat. cr. cou. 1C	UN	1C1	2C				
Koyadora (1970) (E.G. Dt.)	154	18	25	36	—	—	0.047	0.054	78	(51.3%)
Kondareddi (1970) (E.G. Dt.)	137	23	33	15	—	—	0.040	0.050	71	(51.8%)
Kolam (1968) (Adilabad Dt.)	680	68	34	34	—	—	0.015	0 021	136	(20.0%)

An attempt (Table 6) has also been made to compare the tribal data available from the present data with the data available on Kolam tribe from Adilabad district (Chakravartti 1968). While the present data reports a high rate inbreeding in Koyadora and Kondareddi tribes (about 51%). Chakravartti's data reveals a low consanguineous rate of 20% in Kolam tribe. The coefficients of inbreeding for Kondareddi and Koyadora vary from 0.040 to 0.047 (F) and 0.050 to 0.054 (F_1) while those of Kolam tribe are 0.015 (F) and 0.021 (F_1).

Effects of Inbreeding

Inbreeding increases the frequency of homozygotes in a population which are determined by very rare genes. Although sporadic cases of miscarriages, still births, albinism, congenital malformations like digital anomalies are reported in the progeny of consanguineous unions in the present data, for a population such as that of Andhra Pradesh, with a high rate of continuous inbreeding for hundreds of years, the effects may turn out to be quite different. It becomes evident that the frequency of detrimental genes could have considerably declined in this population and the effects on mortality and morbidity may not be as large. Unfortunately our knowledge with regards to Andhra Pradesh, on the effect of both mortality and morbidity is woefully inadequate. More large-scale studies are needed, especially to study the early foetal deaths out of consanguineous marriages, fertility, intelligence, adult measurements and effects of maternal inbreeding. These will not only provide empirical risks, but will answer basic questions about whether sporadic cases are associated with inbreeding and how genetic load revealed by inbreeding is expressed in modern populations. Finally, knowledge of the high inbreeding rate in Coastal Andhra Pradesh is valuable, in a practical way, for genetic counselling.

Summary

Out of 1275 marriages recorded among four caste groups and two tribal populations in Coastal Andhra Pradesh, 498 are consanguineous (39.1%), which include 15.5% matrilateral cross-cousin type, 11.6% uncle niece type and 9.5% patrilateral

cross-cousin type of marriages. The coefficient of inbreeding is found to be 0.035 for autosomal genes (F) and 0.044 for sex-linked genes (F_1).

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INFLUENCE OF SMOKING ON ARTERIAL PRESSURE

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INTRODUCTION

Smoking gives an immediate pleasure. Many people get a definite 'lift' from smoking a cigarette which comes from the pharmacologically stimulant activity of nicotine. One way in which nicotine may provide this 'lift' is by stimulating the smoker's adrenal gland to excrete a hormone (epinephrine) which in turn stimulates the production of glycogen (blood sugar) thus giving the smoker renewed energy. It has been suggested that this rise in blood sugar is a source of considerable part of the gratification produced by smoking (Eysenck, 1965).

Some early studies suggest that smoking also increases arterial pressure (Hallis, 1934).

It is well established that certain morphological and physiological characters positively contribute a continuous variable with a bimodal or trimodal distribution. Measurement of arterial blood pressure of individuals in a given population shows a continuous distribution of both systolic and diastolic pressures. In early studies, a single dominant gene was suggested to explain essential hypertension. However, Pickering et al (1954, cited by Stern, 1960) suggested polygenic inheritance.

THE PROBLEM

The present study is intended to investigate the immediate change in arterial pressure after smoking, which may be considered as an environment created by man himself.

MATERIALS AND METHOD

The materials were collected from 128 males from Cuddapah District of Andhra Pradesh. The subjects were

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unrelated college students of Government College, Cuddapah ranging between 17 and 22 years of age. All of them were habituated to smoke a minimum of five cigarettes per day, regularly, since a minimum period of two years.

The arterial pressure was measured with the help of Baumanometer employing the combined auditory-tactile method.

Every subject was first allowed a rest of 15 minutes and then the arterial pressure was measured from the right hand in sitting posture Then the subject was asked to smoke a cigarette up to a given mark (the brand name of the cigarette was used as a mark and the same brand was used throughout the study). Immediately after smoking, the arterial pressure was again measured from the same hand in the same posture. While measuring the pressure before and after smoking, the first reading was always discarded and the subsequent constant reading was taken into account.

The pulse rate was also noted before and after smoking.

Results and Discussion

The results are presented in Table 1. It is observed that 75.8% of the subjects show rise of systolic pressure. The rise of this pressure ranges between 1-30 mm Hg. However, only 0·8% of the subjects show an increase of 26–30 mm Hg. while a majority of 43.7% showarise of 6.10 mm Hg.

TABLE 1

Rise of Systolic, Diastolic Pressures and Pulse Rate

Units mm/Hg. for arterial pressure and numbers for pulse rate	Rise of systolic pressure No.	Rise of systolic pressure %	Rise of diastolic pressure No.	Rise of diastolic pressure %	Rise of pulse rate No.	Rise of pulse rate %
0	31	24.2	36	28.1	11	8.6
1 – 5	16	12.5	20	15.6	20	15.6
6 – 10	56	43.7	53	41.4	43	33.6
11 – 15	10	7.8	5	3.9	28	21.9
16 – 20	12	9.4	12	9.4	19	14.8
21 – 25	2	1.6	—	—	4	3.1
26 – 30	1	0.8	2	1.6	1	0.8
31 – 35	—	—	—	—	—	—
36 – 40	—	—	—	—	2	1.6

A View of the Symposium Session held at Andhra Medical College, Visakhapatnam

The rise of diastolic pressure is observed in 71.9% of the subjects. The rise of this pressure ranges between 1–30 mm Hg. Only 1.6% of the subjects show the highest increase of 26–30 mm Hg. while a majority of 41.4% show an increase of 6–10 mm Hg.

Increase of pulse rate was observed in 91.4%. A majority of 33.6% show rise of 6–10 times increase while only 1.6% show the highest increased rate of 36–40 times.

Conclusion

The influence of smoking on arterial pressure was studied in 128 males. It is observed that smoking increases both systolic and diastolic pressures, usually between 6–10 mm Hg. However, it may increase up to 26–30 mm Hg. The pulse rate also behaves in the same direction.

Acknowledgements

The author expresses his indebtedness to Dr. M.R. Chakravartti, Department of Anthropology, Andhra University, Waltair for his kind help in preparing this paper. He is thankful to the Principal and students of Government College, Cuddapah for their co-operation.

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GAUCHER'S DISEASE — AN IN-BORN ERROR OF METABOLISM (A CASE STUDY)

K. SRINIVASA RAO
(Department of Pathology, Andhra Medical College)

Philip Charles Ernst Gaucher in 1882 described a case of the disease which today bears his name. It is a rare familial in-born error of the Cellular Metabolism of the Lympho-Haemopoitic organs. It is characterised by the accumulation and retention of Gluco-cerebroside 'Kerasin' in the reticular cells and histiocytes of these organs. The resulting hyperplasia leads to an overgrowth and enlargement of the spleen, bone-marrow, liver and lymph nodes which are the organs involved in the disease. There are a very few Indian reports on this disease. This is the first authentic case report where the disease was diagnosed antemortem from Bone-marrow Cytology and splenic smears study and histopathology of spleen from King George Hospital, Visakhapatnam.

Case Report

A boy aged 16 years with complaint of swelling in the abdomen and pain. Mass was noted eight years ago in the left side of abdomen and ever since it had been growing in size.

Family and Pedigree Studies

He was the 2nd sibling among 5, having one elder brother, one younger brother and sister. The youngest of the brothers died at the 2nd year with a similar complaint of splenomegaly. Father died of a similar disease five years back. Mother was ill-nourished having splenomegaly suggesting a familial predisposition and consanguinity of marriage present in the parents.

GENERAL EXAMINATION

A moderately nourished Boy of 16 years, stunted growth 4′ .5″, anaemic, not jaundiced, Bitotspots present, skin showed peculiarly greyish Tint, pitting oedema present, Pulse, Temp., B. P. Normal, Examination of abdomen revealed massive splenomegaly about 1″ to the right and 2″ below the umbilicus, almost filling the left half of the abdomen. Firm in consistency, not tender. The liver was palpable 2″ below the right costal margin, firm, not tender, having a smooth surface. Lungs and Brain: Nil abnormal found.

Investigations: TWBC: 5800/cmm. Format ged Test Negative.

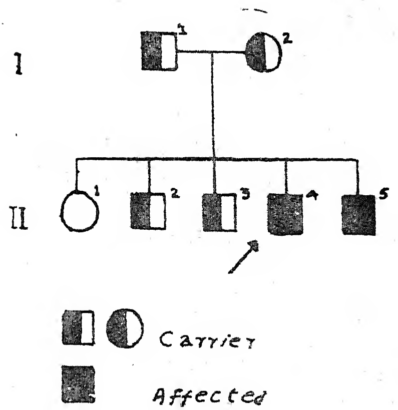

Figure 1

Gaucher's Disease

Liver function Tests: T.T.T. 7 units Serum Bilirubin 0.2 mgm% Z.S.T. 17 units. Vandenburg Test Negative in 1mt.

Cholesterol: 200 mgm.% Serum Acid Phosphotase: 4. K. A. units.

3730/67 Liver Biopsy: Showed a number of Gaucher cells of large size filling the Sinusoids with compression of Liver Cell Cords.

Bone-marrow Smear: (3644/67) showed hyperplasia with normoblasts predominantly with large abnormal pale cells with fibrillary cytoplasm and condensed pyknotic eccentrically placed nuclei 1–2 in number of Gaucher's cells.

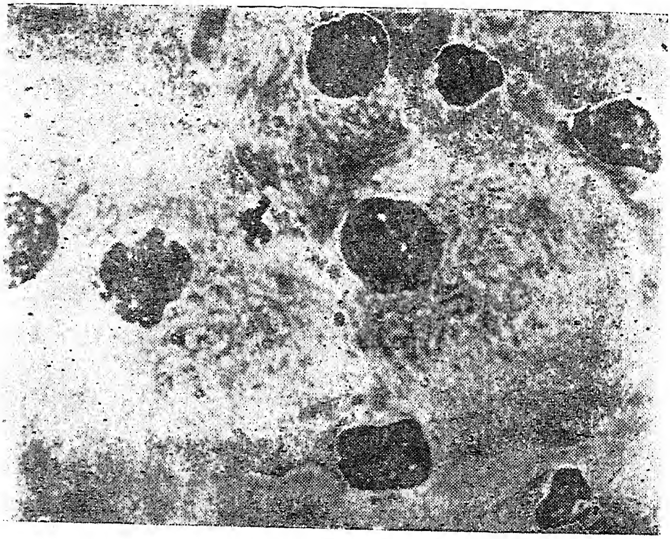

Figure 2
'Gaucher Cells' from Splenic Smears showing Fibrillary Cytoplasm

Splenic Smears: (3999/67) showed large pale PAS (+)ve cells with fibrillary cytoplasm and eccentric nuclei 1–2. These Gaucher's cells predominantly noted.

X-Ray of long Bones: Cortical thinning of lower end of femur with 'Erlenmeyer flask' appearance.

X-Ray Skull: No. abnormality seen.

Haematocrit: PCV: 26% Hb: 8.8 Gms% TRBC: 3.2 millions/cmm. TWBC. 5800/cmm. ESR: 24 mm./1 hour. Diff count: $P_{56\%}$ $E_{15\%}$ $L_{25\%}$ $M_{4\%}$ Late normoblasts, reticulocytes also noted.

MCV: 78 cμ. MCH: 27.5 YYcm.% MCHC: 35% Platelets: 1.8 lacs/cmm. Microcytic hypochromic anaemia picture.

Blood group: 'O'. A.G. Ratio: 2.5/5.0 Gms.%.

Figure 3
'Gaucher Cells' from Liver Biopsy

Splenectomy was done on 24–9–67 and histopathology No. 4833/67 showed. A number of irregular shaped alveolar spaces lined with large Gaucher's cells filling them. The morphology of cells showed fibrillary cytoplasm, PAS(+)ve, Sudan negative and Iron positive cells. The cells were 15–20μ with acidophilic cytoplasm with (H.E. stain). The nuclei were 1–3 in number. There were wide haemorrhages and thrombosis of vessels and fibrosis. Since there are no characteristic changes in Blood chemistry, it is essential to confirm the diagnosis by smears study and histopathology of spleen.

Discussion

Gaucher's disease is best documented for Patients of Askanazic jewish ancestry in the literature mostly, its incidence in Indians and orientals are rarely recorded in the literature. In this Hospital about five cases are noted by us and its incidence is not rare in this Hospital.

The genetic transmission is generally that of an autosomal recessive trait but Hsia et al (1966), suggested that the gene

responsible for the metabolic defect may be transmitted as an autosomal dominant in a few families. Our case report shows clearly the recessive trait both parents are carriers and two siblings of the family were affected with the disease.

Heredity: At least three genetic forms of Gaucher's disease have been described in the literature. The Infantile type is transmitted as an autosomal recessive form. The second type – The Adult type is transmitted as an autosomal recessive which is the usual type. The third Adult type is transmitted as an autosomal dominant. A number of instances have been reported in which Gaucher's disease involves successive generations confirming the dominant character.

The Metabolic Error: It is seen that the Gluco-cerebroside which accumulates in the R. E. Cells of Spleen, Liver and bone marrow arises from a substance called 'Globoside' the major glycolipid of Erythrocyte stroma. As these RBCs become senescent they are trapped and phagocytosed by elements of R.E. system. This Globoside is degraded by a series of hydrolytic enzymes and reactions which result in the sequential release of the four hexose molecules. The primary defect in Gaucher's disease is a deficiency of the enzyme "Gluco-cerebrosidase". It seems reasonable to assume that the splenomegaly and hepatomegaly in this disease are the result of an attempt to compensate for the enzymatic deficiency in this disease resulting in the accumulation of Gluco-cerebroside or Kerasin in the R. E. System. The diagnosis can also be measured by the level of this enzyme activity in samples of Liver tissue and Splenic tissue by needle biopsy.

Summary

A case of Gaucher's disease confirmed by bone marrow study, splenic smear, Liver biopsy and Splenic histopathological Studies is reported. The genetic and familial predisposition of the disease is discussed with the Pedigree of the family studies showing the recessive heterozygous parents and the homozygous affected siblings who manifested the disease process.

The Gluco-cerebrosidase enzyme deficiency is the ultimate enzyme factor which is the 'in-born error'.

Acknowledgement

I wish to thank Dr. N. T. Subramanyam. M.D., Physician, K. G. Hospital and Professor of Medicine for referring this case for detailed investigation.

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A CASE OF XY FEMALE

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In 1948 Gold Berg and Maxwell described a patient with male pseudo hermaphrodite who exhibited a normal female habitus and external genitalia but who had abdominal testes and uterus. In 1953, Morris collected 80 similar cases up-to-date from the literature and discussed the endocrine findings related to it. He coined the term Testicular feminisation syndrome. On occasion the disorder has been termed Gold-Berg-Maxwell-Morris syndrome.

Genetics : Numerous families have been described in which several members of a family were afflicted with the syndrome. It has been estimated that the condition occurs once in every 20,000–62,400 male births. Non-affected female carriers transmit the condition. Most of the available data seem to indicate transmission as a sex-linked recessive characteristic or a male limited autosomal dominant.

A sex-linked transmission is at the basis of the syndrome. A linkage with a known X-linked characteristic would be helpful in proving X-linkage for the TFS syndrome. No color blindness was present in the family.

Boczchowski studied eight families with the Syndrome and reported no close association with the Xg or color-vision loci. Aubert et al on the other hand studied individuals in four generations of a family including eight members with the syndrome and found an association with Daltonism (Red-green color blindness) suggesting a possible X-linkage. Further studies with X-linked characteristics in a large number of families should eventually solve the site of the gene for this Syndrome. Of equal interest is the relationship of the Y-chromosome to the Syndrome. In general Y-chromosome is needed for the development of a testes and a testes will develop even when more than one

X-chromosome is present, as for example in the 47-XXY; 48-XXXY; and 49-XXXXY variations of Klinefelter's syndrome. The testes in turn seems responsible for suppression of the mullerian duct system and for development of male accessory ducts – epididymus and vasdeferens. All of these effects of the Y-chromosome are noted in the testicular feminisation syndrome. In addition the testes in such patients produce androgens.

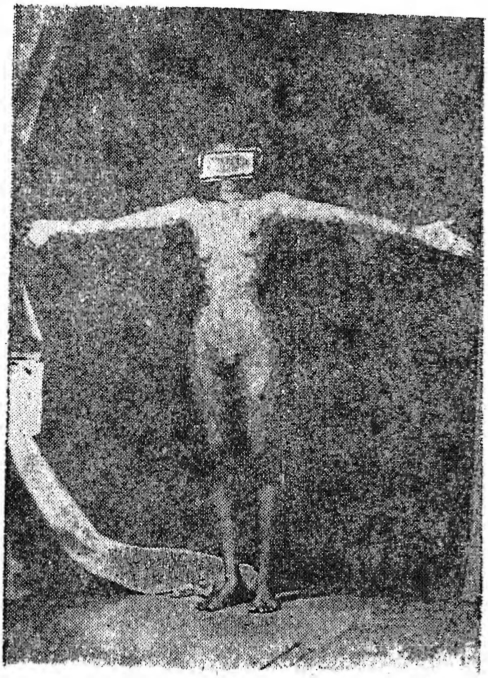

Figure 1

Photograph showing labial bulzes bilaterally of testes in a female phenotype with absence of Pubic and Axillary Hair, well developed Breasts and XY female

One of the most important clinical considerations in this Syndrome is the need to allow the patient to go through puberty before castration. Castration is considered for prophylaxis for neoplasia.

Another consideration of importance involves Genetic counselling – what to tell the patient and her family. Although these patients have a Y-chromosome and testes and would be considered genetically and gonadally to be males – they are nonetheless females with regard to external genitalia general appearance and psychic orientation on a strictly functional basis therefore they are females and must be treated as such. It seems completely unreasonable to make any reference to the 'Male' aspect of the condition to the patient or her family, since all that could possibly come of this would be to create problems for which there are no solutions.

Chromosome Analysis of the Present Case Study

Buccal smears : Study showed 1–3% Barr bodies.

Blood smear : Study showed absence of drumsticks suggesting male configuration.

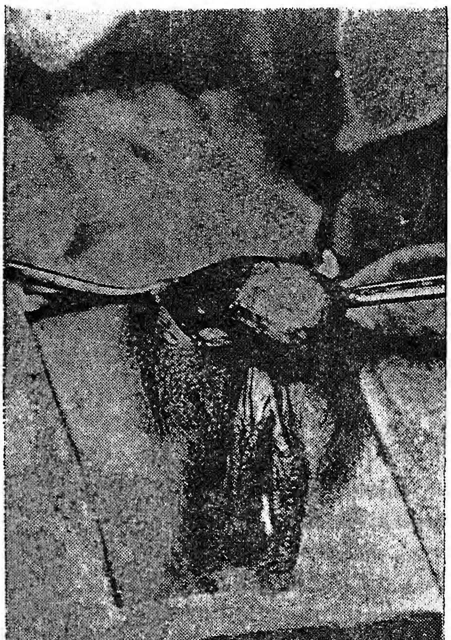

Figure 2

Testes removed from the Labium majors on right side $\bar{c}$ Normal Vagina

Chromosome Culture : Karyotype analysis from Peripheral Blood culture Micro method (T. C. 199) showed 46/XY cell line confirming Male karyotype.

The family is a Hindu, Merchant community. Geographic area : South India – Krishna District. No history of consanguineous marriage in the parents (Figure 4).

Figure 3

Structure of Testes showing sclerased seminiferous Tubules and Leydig cells

The present case is the *2nd child* of the family, 18 years.

Eldest daughter aged 25 years, married, No children. Phenotype : Female – Not available for study.

3rd child is a female aged 13 years has not attained menarche. Phenotype female – Buccal smear and Blood smear negative for sex chromatin.

4th child is 10 years, Male.

5th child is 8 years, Male.

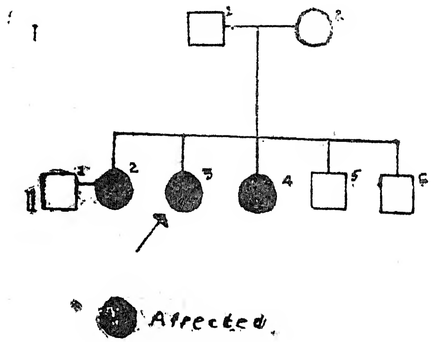

Figure 4
Testicular Feminisation

Case History: Female 18 years – Phenotype female. Genotype: Male – 46/XY.

Examination

General: Tall, female 5′5″, long lower extremities, span longer than the height, well developed breasts, No facial, axillary or pubic hair.

Local: Female external genitalia. Absent Pubic hair. Well developed vagina, mucosa: Rugaose Blind end of vagina ex. absent uterus not felt. bulze in the Rt inguinelabial region. Testicular sensation felt.

Laparatomy: Pelvic gonad – 4 × 2cm × 2cm with short cord – epididynus on the left side; Right gonad – in the labia–majus – Both the gonads appear to be testes.

Histopathology: Capsule T. abuginea thickened Immature Seminiferous tubules; No spermatogenesis noted; Basement membrane of tubules thickened; Leydig cells normal in content confirms the structure of Testes (Immature).

Discussion

In this condition of Testicular feminisation or XY female, despite the presence of testes. The external genetalia and

phenotype is that of normal female. However, the vaginal vault is 2–4 cm deep and no internal mullerian ductal structures can be found. This entity is most likely the result of end organ insensitivity to androgens. This is an inherited condition and a family history as in this case reveal similar affected siblings or maternal aunts, although they feminize at puberty, have primary amenorrhea, no uterus and absence of pubic and axillary hair. The mode of genetic transmission may be X-linked or autosomal dominant. These infants are reared as females and no problem in sex-assignment.

Summary

1. A case of familial, XY female with Testicular feminisation syndrome is presented.

2. The sex chromatin, cytogenetics and histopathological changes of testes were described.

3. Genetic studies of this case discussed.

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GONADO-BLASTOMA ARISING FROM TESTES IN AN INTER SEX WITH CHROMOSOMAL PATTERN OF XO/XX/XY MOSAICISM

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A rare tumor of Gonado-blastoma which is rare and up to 1965 only nine cases have been reported so far. The interest of this paper presents the combination of a rare tumor in a foetal testes on right side with a streak gonad on the left side, with sex chromatin negative in buccal mucosal cells but showing a chromosomal pattern of XO/XX/XY cell-lines (1968).

Case Report

Patient aged 17 years presented with primary amenorrhea.

Figure 1
Eunuchoid Features with Atrophic Breasts and enlarged phallus

She was tall and eunuchoid in appearance. Her growth and mental development was normal. Breasts normal, painful erections of the enlarged clitoris led her to consult the gynaecologist on clinical examination – a clinical diagnosis of Inter Sex was made. An exploratory laporatomy revealed a small uterus and Fallopian tubes. A streak gonad was found on the left side and right gonad was a seat of tumor of testicular tissue – called as gonadoblastoma.

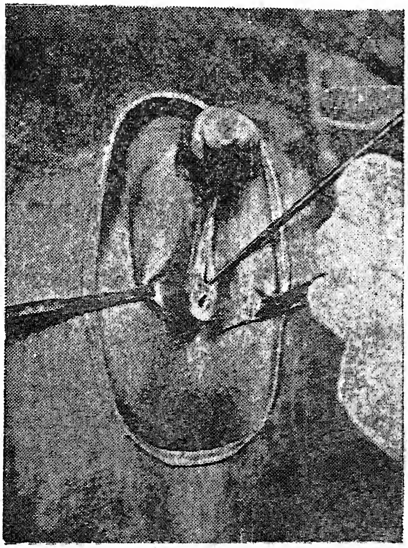

Figure 2

'Intersex' showing enlarged Phallus with Vaginal Orifice

Buccal mucosal cells reported as Negative for Barr bodies. Drumstick count was 3%.

Chromosomal analysis (Sadasivan et al, 1968) revealed XO/XX/XY pattern of Mosaicism of the above case whose clinico-pathological study was made by us.

Mixed gonadal dysgenesis has been used by Sohral (1963) to describe co-existence of streak gonad on one side and testes on the other side.

Figure 3
Tumor 'Gonadoblastoma' with Testicular elements

She was rehabilitated to lead a female life by removal of tumor, clitoridectomy and reconstruction. One year later her general appearance was more feminine and her voice was softer. In the mean time she got married. As she appeared keen on maintaining her feminine role she was maintained on stilbestrol for sometime.

Discussion

The clinico-pathological features and the rehabilitation of a male hermaphrodite to a normal female by genetic counselling and operation in a case who presented with an inter sex with primary amenorrhea. Laparatomy revealed a rare tumor of Gonadoblastoma in a dysgenetic testes. The additional signs of virilism and feminisation can be attributed to androgen and oestrogen secretion from the tumor elements. The rare chromosomal analysis of this case as studied by Sadasivan et al (1968), to be of XO/XX/XY. The patient was rehabilitated as a female by removal of the enlarged phallus and female phenotype was fully restored by cyclical oestrogen therapy. Although Psychological readjustment was slow it was complete and she achieved a completely female sexual life.

Panel Discussion on Research Methodology
in Human Genetics

Summary

A rare tumor of Gonadoblastoma in a dysgenetic gonad with Inter Sex and chromosomal pattern of XO/XX/XY in a case was discussed.

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A CASE OF ALKAPTANUREA

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(Dept. of Pathology, Andhra Medical College, Visakhapatnam-2)

Alkaptanurea is a simple autosomal recessive trait. Certain pedigrees showing Dominant Inheritance were also reported. The earliest description of inheritance of Alkaptanurea was made by Sir Archibald Garrod in 1902 when he showed that the condition is congenital and familial and that it tends to occur with greater frequency among the offspring of consanguineous marriages. The condition appears to be transmitted as an autosomal recessive in most of the Alkaptanuric families. This disease is also an Inborn error of Metabolism chracterized by inability of the subject to reduce homogentisic acid in the urine (Alkaptanurea) leading to pigmentation of the tissues (Ochronosis) and degenerative arthritis and spondylosis. This is said to occur 1 in million subjects and is usually transmitted as a Mendelian recessive character (Stern 1949). Such a rare disease with different hereditary aspects from the usually described features in the literature were being presented in this paper:

Case Report

A man aged 33 years was admitted on 4-10-65 in the N.S. Unit of King George Hospital, Visakhapatnam for low backache of two years duration and pain along the right lower limb acutely since 15 days. The patient has been developing a progressive stoop for the past two years and he has been unable to lie down in bed or stand erect. Black staining of his underwears was noticed from the 3rd month of his age.

Hereditary Aspects and Pedigree

There was no consanguinity between his parents. None of the other siblings suffered from Alkaptanurea. He is the third

in the siblings (Fig. 1). Five children for his parents. Father was treated for diabetes at his 30th year and died at his 50th year. He also had his diapers stained black at his young age. Generally these cases are mistaken for diabetes as it reduces the Benedicts reagent suggesting probably his father was mistakenly diagnosed for diabetes. This familial predisposition indicates the dominant nature of the condition in this case and the absence of consanguinity clearly rules out the heterozygous recessive character in this case.

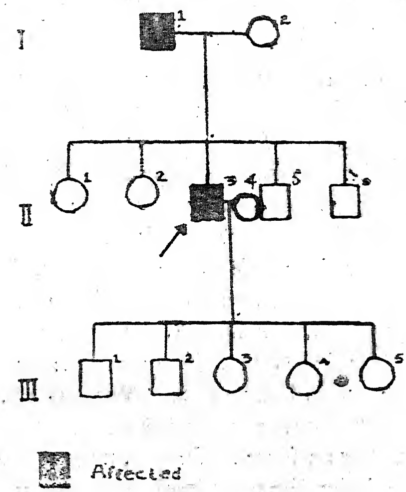

Figure 1
Alkaptonuria with Ochronosis

Investigations

Routine urine analysis only revealed the diagnosis of Alkaptanurea in this case that his urine rapidly reduced Benedicts reagent to black color. Blood examination was in normal limits. CSF was normal.

X-Ray of Lumbar Spine and Dorsal Spine

Showed Osteophytosis, narrowing of I.V. discs and calcification of all Intervertebral discs suggesting Ochronotic spondylosis. He had lumbar disc prolapse also.

Discussion

In 1932 Hogben et al similarly reported from the review of cases and confirmed nearly in all the families. They noted that the higher incidence in males were more often the probands in affected families. He also reviewed that some Dominant trait for Alkaptanurea had to be considered. In a family studied by Pieter the author compelled to conclude that the dominant type of Alkaptanurea existed.

The suggestion by Milch et al that Alkaptanurea is inherited as a dominant gene with incomplete Penetrance was made and cannot be excluded.

In Alkaptanurea homogenitisic acid, the Intermediate metabolic product of Metabolism of tyrosine and phenylalanine cannot be further metabolized due to a deficiency of the enzyme homogenetisic acid Oxidase (Nyhan 1963). Homogenetisic acid therefore collects in the blood and is excreted in the urine. Although this condition is present from birth it may remain unrecognised till middle life when it is often discovered accidentally during a routine examination of the urine as in this case also. Ochronosis is usully recognised in the 4th decade of life, is due to the deposition of the oxidized polymer of the metabolite in the ground substance. Various other tissues like cornea, sclera, conjunctiva, cartilages of the ear, nose, joints, vertebral column, are affected. The pigment is black in colour. The third stage of the disease namely the arthritis and spondylosis develops with advancing age.

Summary

1. A case of Alkaptanurea with autosomal dominant gene with no history of consanguinity is being presented here differing from the literature of its usually being transmitted as a Mendelian recessive character.

2. This case manifested Alkaptanurea, with ochronosis and arthritis and spondylosis, all the three stages being manifested in this case.

3. This disease is recognised during the routine urine examination.

ACKNOWLEDGEMENT

I wish to thank Dr. S.B.P. Rao, M.S., Neurosurgeon of this Hospital and Professor of Neuro Surgery, A.M. College for sending this patient for routine laboratory investigations.

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66. Dr. D. Raghavendra Rao ,,
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80. Dr. S. Bharathi ,,
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86. Dr. J. Veeraswamy ,,

87. Dr. G. Ramaiah Chetty ,,
88. Dr. C. P. Viswanadham ,,
89. Dr. G. Nirmala ,,
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91. Dr. E. Annapurna ,,
92. Dr. R. V. G. Rama Sastry ,,
93. Dr. Lakshmanachari ,,
94. Dr. D. R. Chitra ,,
95. Dr. Ramana Murty ,,
96. Dr. Santi Swarup ,,
97. Dr. I. Dinakar ,,
98. Dr. J. Subbarao ,,
99. Dr. B. Sundareswar ,,
100. Dr. V. Sarvalakshmi ,,
101. Dr. D. S. B. Patnaik ,,
102. Dr. A. Lakshmanarao ,,

Sub-Committees

1. **Reception**: Information Desk.

Chairmen: 1. Prof. T. V. Avadhani (A.U.); 2. Prof. K. Srinivasa Rao (A.M.C.).

Members: 1. Mr. M. Kodanda Rao; 2. Mr. M.D.T. Gopal; 3. Mr. P. Malleswara Rao; 4. Mr. A. Ramesh; 5. Mr. Satyanarayana Rao.

2. **Accommodation**:

Chairmen: 1. Mr. M. Gopalakrishna Reddy (A.U.); 2. Prof. M.S. Radhakrishna Naidu (A.M.C.).

Members: 1. Sri Chalapathi Rao (A.U. Engineer); 2. Dr. R.V.R. Chandra Sekhar Rao, Warden, A.C. and L. Hostels; 3. Mr. D.L. Prasada Rao; 4. Mr. B. Bhaskara Rao; 5. Mr. N. Venkatappaiah; 6. Mr. Y. Sambasiva Rao; 7. Mr. K. V. Satyanarayana Rao.

3. **Food**:

Chairmen: 1. Prof. B.S. Murty (Principal, A.C. and L. Colleges); 2. Dr. M.N. Sastry (Warden, Sc. Hostels).

Members: 1. Sri G. Golla Reddy; 2. Sri D.V. Raghava Rao; 3. Sri A.V. Subba Rao; 4. Sri V.S. Suryanarayana.

4. **At Home (Reception):**

Chairman : Prof. K. Hanumantha Rao (A.U.)

Members: 1. Mr. T. Venkateswara Rao; 2. Mr. M.V.T. Raju; 3. Mr. B.V. Saradhi; 4. Miss A. Padmavathi; 5. Mr. A.N. Syamala Rao.

5. **Transport Committee:**

1. Mr. A.M. Reddi; 2. Mr. M. Satyanarayana; 3. Mr. Rayapa Raju; 4. Mr. M.V. Suryanarayana Raju.

6. **Symposium** :

Chairmen: 1. Prof. J. Venkateswarlu (A.U.); 2. Dr. D. Raghavendra Rao.

Members: 1. Mr. P. Veerraju; 2. Miss D. Lakshmi; 3. Miss K. Anuradha; 4. Mr. B.V. Saradhi; 5. Mr. U.V. Krishna Rao.

7. **Entertainment**:

Chairman : Mrs. L. Bullayya.

Members: 1. Mrs. V. Chandramouli; 2. Mrs. R. Chakravartti; 3. Mr. Mantri Sreenivasa Rao; 4. Mr. K. Venkateswara Rao.

8. **Souvenir**:

1. Sri B. Muthuswami; 2. Dr. (Mrs.) V. Sarvalakshmi; 3. Mr. M. Kodanda Rao; 4. Mr. Gangadhar.

9. **Volunteers**:

President and Secretary (Arts, Commerce and Law).

10. **Publicity**:

1. Mr. V. Venkata Ramana; 2. Mr. T.L. Narsimha Rao; 3. Mr. L. Sambasivarao; 4. Miss K. G. Sundaramma; 5. Miss D. Hymavathi; 6. Mr. D.H. Bhaskara Rao

11. **Excursion**:

Chairman: Sri V. Chandramouli, I.A.S.

Members: 1. Mr. N.V. Kameswara Rao; 2. Mr. R.V. Ramana Murty; 3. Mr. V. Venkateswarlu; 4. Mr. J. Bala Rama Prasad.

12. **Secretariat :**

1. Mr. P. Veerraju (In-charge) ; 2. Mr. M.D.T. Gopal ; 3. B. Bhaskara Rao ; 4. Mr. T. Venkateswara Rao ; 5. Mr. M. Satyanarayana ; 6. Miss Y. Renuka; 7. Miss V. Philomina.

i. *Post office* :

1. Mr. B. Bhaskara Rao (In-charge) ; 2. Mr. N. Narasinga Rao ; 3. Miss D. Bhagya Lakshmi ; 4. Miss M. Sita Rajya-Lakshmi ; 5. Miss B. Nirmala Rani ; 6. Miss A. Mrinalini Devi ; 7. Miss K. Vijaya Lakshmi ; 8. Miss M. Vidyavani ; 9. Mr. A.V. Redy Pantulu.

ii. *Informatian Desk* :

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iii. *Reception Counter* :

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iv. *Lounge* :

1. Mr. T. Venkateswara Rao (In-charge) ; 2. Mr. Ch. V.V. Narasimha Rao ; 3. Mr. K. Manmadha Rao; 4. Mr. K. Satyanarayana Reddi ; 5. Mr. K. Srinivasa Murty 6. Mr. K.V. Rama Reddy ; 7. Miss P.S. Lakshmi ; 8. Miss D. Vijaya Ratnam.

v. *Registration Counter* :

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